THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. 46 SEPTEMBER, 1941 No. 3

THE SURGICAL TREATMENT OF POST-IRRADIATION NECROSIS*

By ERNEST M. DALAND, M.D.
BOSTON, MASSACHUSETTS

IN THIS paper we have dealt only with the actual necrosis of tissues following irradiation and have not considered the late malignant changes following therapy.

Necrosis of tissues is often the result of a radiologist's serious attempt to eradicate a cancer. Due to the great variation in the sensitivity of a cancer to irradiation it is not possible to determine what dosage will be needed to destroy it. It is therefore necessary to continue the treatment until results are obtained. Consequently the normal tissues which make up the bed in which the tumor lies may receive a lethal dosage.

However, necrosis may be the result of careless or unintelligent therapy. We see late necrosis occurring in the first generation of roentgen-ray workers, but this was due to lack of understanding rather than to carelessness. Improper dosage, the wrong filter or failure to use a filter, improper protection, lack of understanding of the physical agent used may all be causes of the destruction of tissues. We have recently seen an acute roentgen-ray burn with necrosis in an interne who used the roentgenoscope for ninety minutes in setting a fracture.

Irradiation over an area previously operated on may cause necrosis because of the impaired blood supply. Ligation of a large vessel supplying an irradiated area may cause lethal damage to the entire area. Sepsis entering the irradiated area may cause a slough. Probably the commonest cause is the injudicious use of roentgen radiation over a section of skin already damaged by previous therapy.

After there has been damage to the blood supply, skin, fat, fascia, periosteum, bone and cartilage are the tissues most likely to undergo necrosis, while muscle is the least damaged. Death of tissues may follow quickly after treatment or may be delayed for a year or two. When it does occur, it is accompanied by severe pain and the surgeon or neurosurgeon may be called on to help relieve it.

In general, the surgical treatment consists in the radical removal of all the necrotic tissue with a wide enough margin to insure an adequate circulation. Removal of the central area of necrosis may give relief from pain but granulations will not appear and flaps will not "take" unless normal tissue is exposed around the periphery. There are times when it is advisable to do no active surgery for necrosis. This applies to regions where bone or fascia cover important tissues and removal of these materials

* From the Pondville Hospital and Cancer Section, Westfield Sanatorium (Massachusetts Department of Public Health), and the Massachusetts General Hospital. Read at the Twenty-fifth Annual Meeting, American Radium Society, New York, N. Y., June 10–11, 1940.

will expose structures which cannot be covered. Exposed bone which can be kept dry may sometimes need no treatment.

CASE I. S. M., aged eighty-two, was referred to me for treatment of a necrotic area of the temple following repeated doses of radium and roentgen radiation. The skin and fat were broken through and the fascia was beginning to slough. Surgery would have involved wide excision and dissection down to bone. Had the bone sequestrated, the temporal fascia would have been the next layer to slough.

Instructions were given a member of the family to dress the wound daily and to remove fascia as it became necrotic. After three months complete healing had taken place.

CASE II. I. L., aged thirty-three, was seen in March, 1933, for a carcinoma of the auditory canal, recurrent after two operations. With the assistance of an otolaryngologist all involved tissue was exposed through an incision in the posterior part of the ear and the whole cartilaginous canal was removed by electrocoagulation. The drum was not involved and was not destroyed. The anterior wall of the mastoid bone was involved and this was coagulated. Eight radium needles with 0.25 mm. platinum were placed in the canal for twenty hours (800 mg-hr.) and the following month high voltage roentgen therapy, 1,500 r, was given to the ear and mastoid region.

Six months later we noted a large amount of exposed irradiated bone, but it was a year before any bone came away. Two years after operation a recurrence was noted overlying the drum. Further electrocoagulation was done and again small needles (600 mg-hr.) were inserted against the drum.

It is now nearly five years since the last operation and at least one-half of the exposed bone is still present. The anterior bony wall has crumbled away, allowing the condyle of the mandible to subluxate posteriorly. Parts of the mastoid bone are still exposed and others have become covered with epithelium. There is some loss of hearing, but there is practically no bone odor and she has no pain. In this case we have irradiation osteitis still present seven years after treatment. Many attempts have been made to remove the surface of the bone with rongeurs, but the bone is eburnated and shows no attempt at sequestration. It seems safer to leave this bone to protect more vital structures.

CASE III. M. T., female, aged seventy-two, was seen on October 20, 1930, with a recurrent carcinoma of the outer canthus, lower lid and face. She had had two series of radium treatments but the disease persisted. Excision was done with closure by a plastic procedure. Two years later a nodule appeared over the lower edge of the orbit and malar bone. A radium pack was ineffective. Platinum walled radium needles were inserted and a dose of 480 mg-hr. given. Double this dosage was given three months later and the same dosage six months later, with final destruction of the tumor. In January, 1934, six months after the last treatment, examination showed complete loss of all tissue down to bone in the irradiated area.

For five years the condition remained the same with an area of exposed malar bone 3×2 cm. There was no pain and no discharge but the skin edges were tending to pull away from the bone. The patient died at the age of eighty-two without further recurrence.

Any operation to remove this bone would have been extensive and the antrum would have been opened. Conservative treatment made it possible for the patient to live in comfort.

NECROSIS OF CARTILAGE

Modern technique has nearly done away with the terrors of necrosis of cartilage. It was such a serious problem a few years ago that surgeons advised operation rather than see the patients suffer from radiation therapy. I recall the case of a physician with a keratosis on the upper border of his ear. It was treated with a bare tube of radon with small dosage but he developed a chondritis and begged for surgical removal which gave him relief. Now we see carcinomas involving the entire ear being treated by high voltage roentgen therapy with proper filters and the treatment carried out over several weeks, all without chondritis and without pain. The same is true of carcinoma in the region of the alar cartilage, as that area was formerly a bugbear for the radiologist.

This does not mean that necrosis of the cartilage cannot occur. The following case is illustrative.

CASE IV. A. B., aged fifty-nine, was first seen in the cancer clinic of the Westfield Sanatorium

on June 15, 1938, with a mixed basal and squamous carcinoma of the bridge of the nose of ten years' duration. He was given 4,800 r with 200 kv. at 25 cm. and 1 mm. Al filter at one sitting. The lesion had completely healed in six weeks but there was edema and redness of the septum. Fourteen months later he complained of excruciating pain in his septum and shortly after a perforation appeared with relief of his pain. Here was definite destruction of cartilage appearing sixteen months after therapy.

NECROSIS OF THE SKULL

Irradiation osteitis of the skull is not the same problem as simple osteitis of the skull. In the latter condition the destruction is usually limited to the outer table. Given sufficient time the outer table which has been bared of its periosteum will separate and come away or it may be chiselled off. The diploë supplies sufficient blood supply to send up new granulations and the defect is gradually closed in. In irradiation necrosis it is not possible to separate the outer table from the inner, nor is it advisable to bore holes in the bone to aid the formation of granulations. Two failures are cited.

Case v. G. F., aged sixty, who had developed carcinoma in an old burn of his scalp, was seen several years ago at the Collis P. Huntington Hospital. The carcinoma was excised and the defect satisfactorily grafted. Several years later he returned with a new cancer in another part of the scalp. Deep roentgen therapy was given with poor results. The lesion was then excised surgically down to the bone. Later an attempt was made at removing the outer table which showed no evidence of reaction from treatment, but instead the whole area of bone had to be removed. Beneath the bone the dura showed reaction. It was not possible to close the defect, but as long as wet dressings were continued the dura appeared healthy. The patient left the hospital and stopped the dressings and when he returned the dura was like leather. He died of "a shock" three months later. As the limbs involved were contralateral to the defect, we believe he had an area of softening of the brain beneath the exposed area.

Case vi. S. H., aged eighty-two, was admitted to the Pondville Hospital, November 18, 1937, with a carcinoma of the forehead, recurrent after repeated treatments with roentgen rays and radium. The lesion was excised by electrosurgery down to bone, but as the bone appeared normal, this was not coagulated or removed. One month later fifteen drill holes were made through the outer table until slight bleeding occurred—the usual sign that the diploë has been reached. However, no granulations ever appeared in the holes. Since then the whole bone has shown the usual characteristics of irradiated bone and has gradually crumbled away.

From these cases it is evident that the skull receives its full share of damage when irradiation is used on the scalp. Wherever possible surgery should be used as a primary measure, for it is unsatisfactory as a secondary measure.

NECROSIS OF THE JAW

Cancer of the buccal mucosa and tongue with involvement of the jaw bones is an ideal condition to bring on necrosis following irradiation. The greater the degree of sepsis in the mouth and the poorer the condition of the teeth, the greater is the amount of necrosis and pain. Small areas of necrotic bone should be resected. We have sometimes used electrocoagulation to change irradiated bone to bone destroyed by heat and it then comes away.

Case vii. J. K., aged sixty-three, was first seen at the Pondville Hospital on January 19, 1928, with an extensive carcinoma involving the left lower jaw and extending back to the anterior pillar and with induration extending into the submaxillary region. Roentgen examination showed bone destruction. The patient's mouth was fairly clean, and edentulous. Gold radon seeds were inserted into the tumor and deep roentgen therapy was given externally. A total of 1,200 r was given at this time with 900 r three months later. There was good response to the treatment. Three months later bare bone was visible and he had a large opening in his cheek (Fig. 1).

For the next seven years the necrotic bone continued to come away. The bone was rongeured many times and numerous attempts were made to close the fistula. There was never any reappearance of the cancer. In May, 1935, the fistula was closed successfully and the last

FIG. 1. Case VII. Necrosis of the jaw following irradiation of carcinoma of the buccal mucosa.

bit of exposed bone came away (Fig. 2). The patient died without recurrence in 1938 at the age of seventy-three.

This was a typical example of bone necrosis from irradiation. There was never any attempt at sequestration of the bone. Sepsis was relatively mild and the amount of pain was not great. For several years we have laid a good deal of emphasis on oral hygiene before attempting any surgery or irradiation for lesions of the mouth. It is our practice to have a dentist survey the mouth and remove such teeth as are carious or infected before any irradiation is given. Several days are allowed to elapse after extractions, and irrigations and mouth washes are used to clean up the mouth. In the following case this preliminary therapy was not given.

CASE VIII. S. L., aged fifty-two, was admitted to the Westfield Sanatorium April 18, 1938, with a carcinoma of the base of the tongue. Irradiation was given to the lesion through two neck portals and through another left submaxillary portal with excellent regression of the lesion. Three months later a dentist noted that several teeth should be removed, but, as these were in the irradiated area, this was not thought wise. One year later a loose tooth was removed without anesthesia. For several months thereafter the patient had severe pain in the jaw but he became free from pain when several sequestra came away.

In this case the bone condition was a simple osteitis from infection and not one of radiation osteitis. Much pain would have been spared had he had proper attention early. We now believe that all teeth in the path of the irradiation should be removed unless the teeth can be protected as in treatment of a lip. We do not insist on the removal of contralateral teeth. After treatment has been given no further extractions should be done for at least two years and then complications may occur as shown in the next case.

CASE IX. J. E. (Pondville Hospital, 1916, and Westfield Sanatorium), aged thirty-nine, was admitted January 30, 1930. Examination

FIG. 2. Case VII. Result after repeated attempts to close the defect in cheek.

showed a large tumor mass in the region of the right tonsil, bulging over to the midline and extending through the neck to the parotid region where it was palpable below the angle of the jaw. Biopsy showed a mixed tumor of the parotid.

He was given an external radium pack of 1,000 mc-hr. at a distance of 5 cm. with 2 mm. lead filter. He also received 1,584 mc-hr. in the form of gold radon seeds directly into the pharyngeal tumor. One year later no tumor could be seen from within but one nodule remained externally. He received more gold radon seeds and radium needles were inserted, giving the equivalent of 1,180 mg-hr. There was good regression.

Four years later he returned with recurrences inside and outside the mouth. He was given 900 mg-hr. in platinum needles. This was followed by 2,000 r to the external mass.

Six months later several teeth on the right lower jaw were extracted. During the next year numerous sequestra came away from the jaw and an external sinus developed.

He was last seen in March, 1940, and no recurrence found. There has been no further necrosis of the jaw during the past three years.

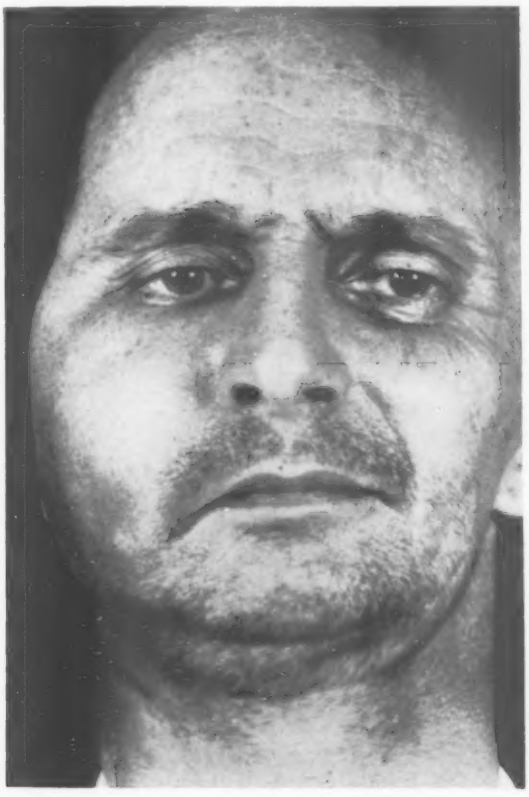


Fig. 3. Case x. One week after ligation of external carotid artery showing marked edema and swelling of entire irradiated area.

Fig. 4. Case x. Condition eleven days later. The entire irradiated area is gangrenous.

Microscopically any tissue which has undergone extensive irradiation shows extreme fibrosis and endarteritis. Late sloughs are due to insufficient blood supply. If anything is done to decrease the circulation further, necrosis may be hastened as is shown in Cases x and xi.

Case x. A. C., aged fifty, was seen at the Massachusetts General Hospital in August, 1937, with a carcinoma of the buccal mucosa. He received 7,100 r high voltage roentgen therapy over a period of one month. After these treatments had been started he went to his dentist and had some teeth extracted. Two months later he had a severe hemorrhage from the cheek and had an emergency ligation of the

Fig. 5. Case x. Condition eight days later
The gangrenous area has been removed.

external carotid artery. Within a few days there was evidence of circulatory change and he was referred to the Pondville Hospital on December 20, 1937. There was marked edema and swelling of all the area which had been irradiated. Figures 3, 4, 5 and 6 demonstrate the rapidity of the changes in the irradiated area, for all the treated tissues were destroyed.

In spite of the large amount of therapy which he had received, a recurrence developed along the jaw and extended to the tonsil. Death occurred within a few weeks.

Case xi. J. L., aged forty-nine, was admitted to the Pondville Hospital July 25, 1935, with an extensive carcinoma of the floor of the mouth with metastasis in the neck. All of his teeth had been removed three months before. He received 3,200 r deep roentgen therapy to the right side of the neck and jaw and 2,600 r to the left side, given in two series. There was apparently complete disappearance of the primary tumor and marked decrease in the size of the nodes. However, a few weeks later he had several hemorrhages from the mouth and was readmitted to the hospital. The right external carotid artery was ligated.

Following operation there was no change in the condition of the irradiated area until four weeks had elapsed. He then developed edema and swelling of the side of the face and six weeks after operation an area of slough in the skin appeared. This area increased in size until the entire irradiated area had sloughed (Fig. 7). The jaw became exposed and finally was removed as a sequestrum just one year after the first treatment was given. The carcinoma recurred and he died two years and nine months after treatment.

Sepsis developing in an area of late irradiation fibrosis is another means of producing necrosis by disturbance of the circulation. The following case is identical with the last except that infection rather than ligation caused the necrosis.

Fig. 6. Case x. Condition two weeks later.
The jaw is exposed.

Fig. 7. Case xi. Necrosis of face and jaw following irradiation and subsequent ligation of the external carotid artery.

Fig. 8. Case xii. Carcinoma of buccal mucosa with perforation of the cheek and involvement of the skin.

Fig. 9. Case xii. Infection entering from the mouth and jaw has caused the formation of a large temporal abscess.

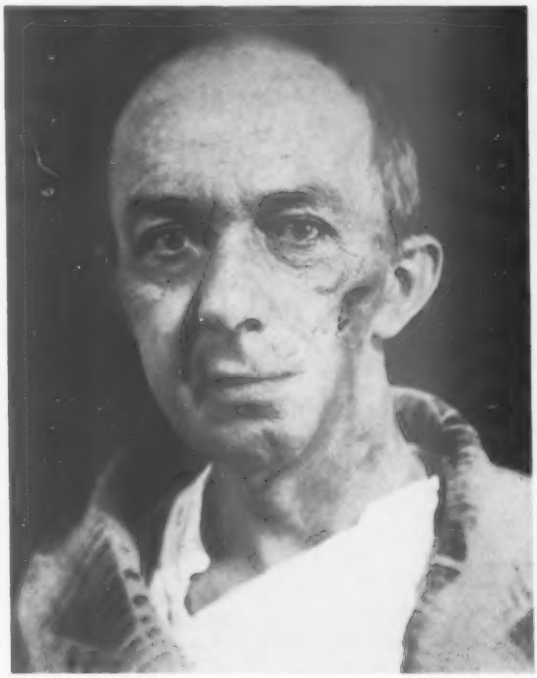


Fig. 10. Case xii. The entire jaw has become separated and has been removed.

Fig. 11. Case xii. *A*, a tube pedicle graft has been prepared. *B*, skin flaps have been turned in for a lining and the tube pedicle has been attached.

Fig. 12. Case xii. *A*, the tube pedicle graft has been detached at the lower end, and the end sutured above the body of the graft. *B*, more scar tissue has been removed, the tube has been opened and the defect closed.

Case xii. H. H., aged fifty-five, was first seen at my office in December, 1933, with an extensive carcinoma of the buccal mucosa and face with perforation of the cheek (Fig. 8). The lesion appeared inoperable and he was referred to the Collis P. Huntington Hospital where he received 2,700 r, deep roentgen therapy, with excellent results. However, the amount of pain which followed treatment demanded hospitalization and he was admitted to the Pondville Hospital on February 27, 1934.

On admission there was extensive slough inside the cheek with no definite active disease. Unfortunately the examining surgeon advised removal of the teeth in this section of the jaw and this was done. Ten days later he developed slight sepsis in the irradiated skin but this cleared up and he went home. Three months later he returned with a marked swelling of the left side of the face and bulging of the temporal region (Fig. 9). He was unable to open his mouth for inspection of the jaw. A few days later a large temporal abscess was drained. One week later the infection spread downward and sloughing occurred of the entire irradiated area (eight months after therapy). Three months later the entire jaw was removed as a sequestrum and the wound cleaned up quickly (Fig. 10).

From March 4 to July 24, 1935, several plastic operations were performed to close the defect. A tube pedicle graft was constructed in the acromiothoracic region. Skin flaps were turned in to line the defect. The final result was rather crude but he was expected to return for further plastics but did not do so. He was alive three years after discharge and says he has had no recurrence, but he has not been examined.

The extraction of teeth in a sloughing mass of cancer doubtless spreads infection into the bone and allows infection to spread along the fascia into the area beneath the temporal muscle. We have seen this occur several times from an ulceration around the jaw. No dental work should be done on teeth which have been subjected to irradiation until at least two years have elapsed. All dental work should precede therapy for the cancer.

Necrosis of Lumbosacral Region

The lumbosacral region appears to be one particularly susceptible to irradiation necrosis. We have seen 4 cases within the past two years.

Case xiii. N. C., aged about fifty, was seen in consultation at the Boston City Hospital in November, 1938. This patient had been operated on in 1937 for a vascular tumor of the spinal cord, thought to be a hemangioma but not proved by biopsy. A midline incision had been made for the laminectomy. In September and October, 1937, he received high voltage roentgen treatments through two 15×15 cm. fields on either side of the scar until 1,470 r had been given to each field. In January, 1938, he received 1,700 r additional therapy to each field. In July, 1938, he developed an ulceration of the irradiated area on one side and shortly afterwards the second area ulcerated.

Examination in November, 1938, showed a large area of bronzing with edema of the skin over the lumbar region. The scar was still healed and there was an inch of thickened skin on either side. Laterally two deep ulcers were seen with destruction of skin and fat down to sloughing fascia.

This was an unusual picture in that the edges of the wound which had been turned back at operation were the healthiest parts, although it was probable that the ligation of vessels near the midline had interfered with the blood supply of the adjacent tissue.

These sloughing ulcers were later excised by another surgeon and the areas later covered with skin grafts. Healing occurred except for several sinuses which were later found to extend to the sacrum and sacroiliac joints.

Case xiv. F. S., aged fifty-nine, a retired school teacher, was seen on November 10, 1938, and admitted to the Baker Memorial of the Massachusetts General Hospital. A tumor of the intestines had been removed in 1926 but no microscopic examination was made. In 1930 a second operation revealed "a very extensive carcinomatous involvement of all the retroperitoneal glands and liver" but no tissue was removed for examination.

From 1930 to 1932 she received roentgen therapy (type and amount unknown) through anterior and posterior portals. In 1934 she developed induration about the umbilicus. This was excised but the wound never healed. Later she developed an ulceration over the sacrum. In the meantime she had noticed enlarged axillary and cervical nodes and as these re-

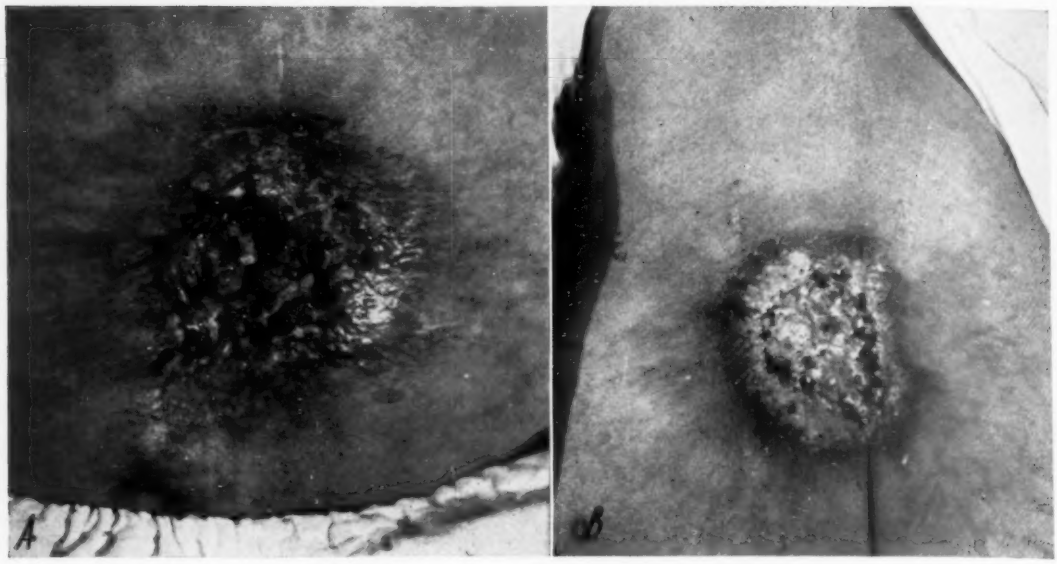


FIG. 13. Case XIV. *A*, irradiation ulcers of abdominal wall about umbilicus; *B*, of sacral region.

sponded to light doses of roentgen rays it was thought probable that these nodes as well as the abdominal nodes represented lymphoma. The ulcer of the abdominal wall had been present for four years and had troubled her chiefly because of the odor. The posterior ulcer, present for three years, gave constant pain.

Examination showed absence of the umbilicus. Surrounding its normal position was an extensive area of irradiation dermatitis with telangiectasis around the periphery and a deep ulcer extending down to the fascia. There was a similar ulcer with less depth over the upper portion of the sacrum (Fig. 13). Operation was advised.

On December 6, 1938, operation was performed on the posterior ulcer. An incision was made around the periphery of the irradiated tissue through normal skin. The wound edges were beveled in to the edge of the normal fat which was entirely absent around the ulcer. One layer of fascia was removed. This left a layer of fascia overlying the muscles. Numerous incisions were made in this fascia to aid the formation of granulations. The fascia had a peculiar gray appearance and did not look healthy.

Two months later there was very little evidence of healing. The wound was covered with a gray hyaline-like scum which could be sep-

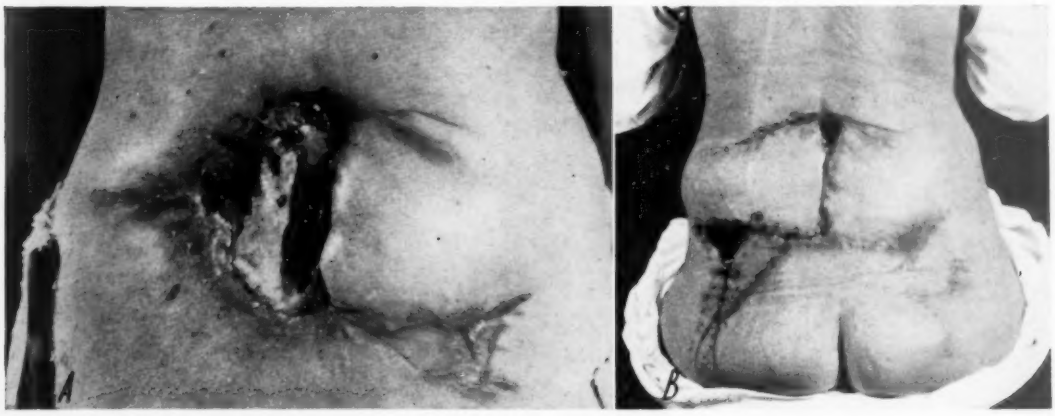


FIG. 14. Case XIV. *A*, the ulcer has been excised. One-half of the defect has been closed by a flap from the buttock. Note the surface film of gray slough. *B*, the remainder of the defect has been closed.

arated with scissors but which reappeared in two or three days. At the time of operation on the anterior wound this surface was again curetted and another layer of necrotic fascia removed down to the sacrospinalis group of muscles. Dakin's solution was found to be the best material to clean up the wound. On March 4 there still was little evidence of healing. The gray film (in some places 1 cm. thick) had reappeared. Again this was removed down to bleeding muscle and the entire area was covered with thick split grafts. Again the wound covered over with the gray slough and the grafts were apparently lost. Five weeks later a more radical method of closure was adopted. A large flap of skin and fat, measuring 7 by 4 inches, was removed from the right buttock and swung at right angles to cover the defect. The surface exudate was again curetted and to our surprise practically all of the skin grafts were present under this hyalinized layer. The grafts were removed and the graft sutured in place. As a result of this operation, one-half the wound was closed (Fig. 14*A*) for part of the graft sloughed and the rest pulled away. At this time it was noted that three spinous processes were exposed along the edge of the flap which stuck down to the muscle readily.

She was allowed to return home for a few months and then reentered the hospital. A large flap was dissected up from the left buttock, the irradiation "scum" and the exposed bone were removed and the flap sutured in place (Fig. 14*B*). This procedure was satisfactory and the wound healed fourteen months after the first excision.

Fig. 15. Case xiv. The abdominal ulcer has been excised and closed by a right angle flap.

During this same period the anterior abdominal wall ulcer was excised and closed by a right angle flap at one sitting (Fig. 15). The necrosis was found to involve all layers of the abdominal wall including the peritoneum which had the typical gray exudate. Very little difficulty was experienced in the healing of this wound.

Case xv. H. S., aged sixty-six, was admitted to the Pondville Hospital on May 8, 1939, with a carcinoma of the skin of the lumbosacral region of fifteen years' duration. Previously he

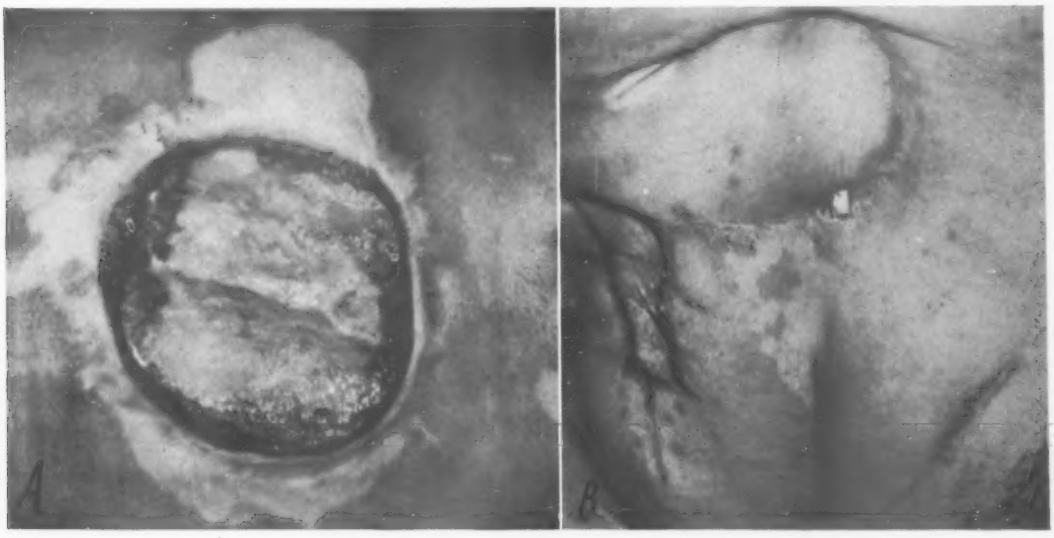


Fig. 16. Case xv. *A*, a large irradiation ulcer has been excised. *B*, the defect has been closed by a right angle flap.

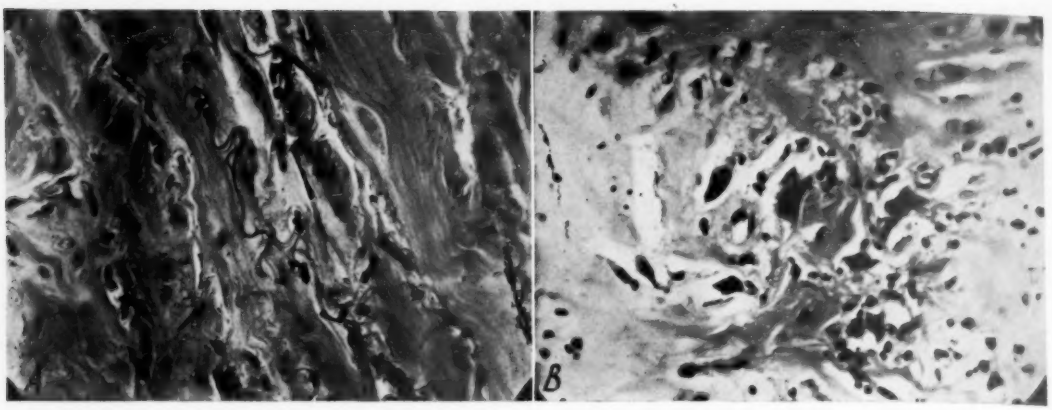


FIG. 17. Case XVI. Photomicrograph of removed irradiated tissue (×400).

had received three courses of roentgen therapy. He was given 7,200 r in eighteen treatments through a small portal. Four months later the entire area was excised (Fig. 16*A*) and persistent disease found. The spinous processes were exposed. Two months later the sloughing fascia and bone were removed and closure accomplished by a right angle flap (Fig. 16*B*). A sinus persisted and recently several pieces of irradiated bone were removed. At this time, it is probable that the meninges were opened, for there was a gush of bloody fluid at operation and this leakage continued for several days. He also had difficulty in emptying his bladder but these symptoms have cleared up and his wound is nearly healed.

CASE XVI. F. W., aged seventy, admitted to the Westfield Sanatorium July 6, 1938, with an ulcerated basal cell carcinoma 5 cm. in diameter, over the right lower lumbar region. He was treated by 200 kv. roentgen radiation and received 4,200 r in daily doses of 300 r, the treatment being completed July 26, 1938. Moderate improvement followed, but five months later there was still activity and 5,200 r additional was given through a 5.6 cm. round cone with 0.5 mm. copper. Healing failed to occur.

On May 16, 1939, a large ulcer 5×6 cm. with a necrotic center was present. The patient complained of pain radiating down the right leg from the ulcer. The ulcer was excised, but it was necessary to remove some of the deep muscle to get bleeding tissue. Still no healing occurred but deep sepsis appeared and the patient died in September, 1939, of acute purulent cerebrospinal meningitis, fourteen months after treatment was started.

The original pathological examination showed basal cell carcinoma. No carcinoma was found in the specimen excised in May, 1939. Microscopically this showed "marked necrosis and ulceration with large masses of bacteria present. Dense, hyaline fibrous tissue below ulceration with swollen fibroblasts visible. Degenerated elastic fibrils. Thickening and hyalinization of arterial walls. Dilatation of capillaries with swollen endothelium present. Scattered lymphocytes and plasma cells. Degenerated striated muscle. Radiation reaction."

NECROSIS OF THE SOLE OF THE FOOT

Irradiation of plantar warts has come to be an accepted method of treatment. Yet it is not without its dangers if the treatment is prolonged or repeated. During the past year we have observed 5 patients with irradiation ulcers on the foot. In each case the original irradiation was effective for a time, but recurrences appeared, further treatment was given and ulceration followed. One patient had an ulcer on each foot.

The secondary treatments have been given from two to eighteen years after the primary irradiation. In several instances trauma and infection have apparently started the ulceration. All of these patients have suffered severe pain and have been unable to bear weight or to walk.

We have observed patients who had had but one series of treatment and have been impressed by the amount of skin atrophy

that they show—more than one sees when a similar treatment is given on the face. In addition to the cases mentioned we have heard of 5 others within the past few months. We doubt if it is safe to repeat a series of treatments.

The surgical treatment of these ulcers has been difficult. In 2 instances the ulcer was deep enough to require removal of a metatarsal. In 2 it was necessary to crush the posterior tibial nerve to relieve pain. The type of graft required depended on the size, depth and position of the lesion and the time involved in repairing the defect varied from one to fourteen months. In each case a persistent wart was found by the pathologist.

Case xvii. T. M., aged twenty-one, was first seen on October 30, 1939. Four years previously he had received roentgen treatment for plantar warts. Several treatments were given at weekly intervals but the type of treatment and the dosage are not known. Three years later the warts recurred and he received 900 r in November, 1938, 900 r in February, 1939, and 1,800 r in May, 1939. High voltage roentgen therapy at a distance of 20 cm. was used. The filter for the first two was 0.5 mm. copper and for the last treatment 0.25 mm. copper.

Following treatment the warts cleared up and the patient spent his summer in active athletics, much of the time wearing sneakers. He knows of no direct trauma but in August a painful ulcer appeared and for four weeks he has been confined to a hospital and has required opiates to relieve his pain.

On November 4 he was operated on at the Baker Memorial Hospital. The lesion was excised down to normal fat. A pedicle graft was lifted from the opposite thigh and sutured in

Fig. 18. Case xvii. *A*, ulcer of foot following irradiation of a plantar wart. *C*, pedicle graft has been raised from the thigh and sutured to the foot. *B*, end-result.

place on the foot. A plaster spica including both legs was applied and this was left in place for two weeks. The flap was then divided and sutured in place on the foot. Weight bearing was started three weeks later and he walked normally two months after removal of the ulcer.

We have seen necrosis of the entire abdominal wall in a man with a retroperitoneal tumor thought to be a fibrosarcoma but which proved to be a dermoid cyst. An exploratory operation has been done and this was followed by a course of deep roentgen therapy. Shortly after a second series of treatments the wound broke open and multiple fistulae appeared. Seventeen major procedures were done to close or short-circuit these fistulae. The patient succumbed some ten years later to a carcinoma of the pharynx.

One unusual complication of irradiation is a fracture in the neck of the femur in a patient who had received prophylactic treatment to the inguinal nodes following amputation of the penis for cancer. Healing has failed to take place in spite of a nailing operation and this must be considered a true case of irradiation osteitis.

The tendons and tendon sheaths on the dorsum of the hands are very susceptible to irradiation. Treatment of small cancers may give undue reactions, while treatment of large cancers may produce such severe necrosis that amputation may be required.

SUMMARY

The ligation or disturbance of the blood supply of an irradiated area, infection reaching this area, or the undue prolongation of therapy after tissue changes are evident, are all conducive to necrosis of the treated area.

All necessary dental work should be done before radiation therapy is started. No extractions should be done for many months thereafter.

Bone with a thin covering is greatly affected by irradiation and when that covering is broken is likely to become necrotic. Separation of the bone may take several years.

The lumbosacral region does not tolerate heavy radiation therapy well. If ulceration occurs, healing is slow and surgical measures are difficult.

Radiation therapy to a plantar wart, which is repeated after an interval of a few months or even years, may cause severe and painful necrosis.

Beneath an irradiation ulcer is found a tenacious, hyalinized area of connective tissue which quickly re-forms after removal unless normal tissues are used to cover it. Pedicle grafts are more satisfactory than skin grafts in closing these defects.

DISCUSSION

DR. DOUGLAS QUICK, New York. In opening the discussion on this paper, I can do little more than compliment Dr. Daland on a very excellent presentation of the subject in such a very brief period of time; and for the most part to endorse just what he has said to us.

I am glad that Dr. Daland has mentioned particularly the influence of infection in causing the breakdown in heavily irradiated tissues. It is surprising how much irradiation tissues will stand and carry through to the final period of stabilized repair, if infection does not supervene. For this reason, it is especially important, particularly in the mouth, to pay careful attention to oral hygiene from the beginning of treatment. The same applies to any area where the total amount of treatment is expected to be very heavy.

I can see Dr. Daland's point in doing all necessary dental work, especially extractions, before instituting treatment to the growth itself. On the other hand, I believe that such delay is open to question. My own feeling is that the mouth in poor hygienic condition, chiefly the result of dental neglect, is one in which the damage has already been done, once growth develops. I believe that treatment of the growth together with very rigid hygienic measures should be gone ahead with concurrently. I refer to frequent periodic irrigations and cleansing of the mouth with sprays under pressure.

In my judgment, this type of treatment should carry on for weeks, or even months after the disease has entirely cleared up, before causing any new break in the continuity of tissues for extractions. Malignant disease in the mouth scarcely warrants waiting until we have carried

through a dental program with subsequent healing. In the extraction of teeth, fresh sockets are opened to the infection already existing in the mouth. This in itself often leads to a low grade infection extending into the bone, thus increasing the hazard of secondary bone necrosis. I much prefer cleaning up the growth and then taking care of the originally neglected dental problem.

I would like to endorse what Dr. Daland has said about using a coagulating current to destroy more quickly limited areas of condemned bone with its accompanying infection. The time of exfoliation of the sequestrum is very much reduced by resorting to this measure and, in fact, a substantial percentage of complete resections can be avoided by resorting to this procedure early in the course of treatment.

The term "coagulation" is used so very frequently in connection with cleaning up these areas of secondary necrosis that I think a proper distinction should be made between the use of a heavy locally destructive current for a bone area, such as I have just referred to, and the finely adjusted cutting current which produces a very thin film of necrosis only and which is better adapted for cleaning away devitalized areas in the soft parts. By using a cutting current of this latter sort, preferably with a fine loop, the soft part tissues can be shaved away in layers. By watching the base very carefully, one can readily determine how far to extend the sacrifice of tissue by this means, the net result being less sacrifice of soft parts, very often, than if the heavier coagulating current is resorted to.

Finally, I should like to endorse very thoroughly what Dr. Daland has said about the use of pedicle flaps wherever possible. I believe the general surgeon doing reconstructive work chiefly with traumatic cases is apt to misjudge the circulation with which he has to deal even far beyond the zone of necrosis, when it comes to dealing with an irradiation ulcer. The principles that would apply in ordinary traumatic surgery are not applicable in dealing with post-irradiation ulcers. The margin of safety is much less in the latter group of cases.

ELECTROSURGERY (ELECTROCOAGULATION, ELECTRODESICCATION) AS AN ADJUNCT TO RADIATION THERAPY IN THE TREATMENT OF CANCER*

By GEORGE E. PFAHLER, M.D., Sc.D., *and* DAVID A. SAMPSON, M.D.
PHILADELPHIA, PENNSYLVANIA

ELECTROSURGERY has a definite field of usefulness as a supplementary measure in the radiation treatment of many benign and malignant lesions. We are under the impression that many radiologists are not fully aware of the value of this method, thereby failing to avail themselves of all weapons in our armamentarium. Some other radiologists, while cognizant of what can be accomplished by this procedure, have been in the habit of considering such forms of treatment beyond the scope of (and possibly beneath the dignity of) radiologists. This has led them to refer occasional patients to physiotherapists or to surgeons for electrosurgical procedures, but for the great majority of cases, it has actually resulted in omission of this sometimes very useful treatment. In the management of cancer, it is the duty of every one of us to utilize every means available, not only in curing or palliating cancer when it has developed, but also in preventing cancer. One of us (Pfahler) has been using this additional method since 1910 and we are convinced that it has great value. In the hope of stimulating interest in electrosurgical procedures which can be legitimately carried out within the domain of radiotherapy, we are prompted to present some of our experiences, some of our observations, and the results as well as recommendations concerning technique and general management. The late William L. Clark deserves much credit for the development of the method of treatment and it was the privilege of one of us (Pfahler) to be rather closely associated with him in his early work.

The eradication of moles and warts, though actually benign lesions, legitimately comes within the scope of the radiotherapist. Being abnormal structures, and actually tumors, they are precursors of numerous carcinomas. The story of the benign mole or wart, repeatedly tramatized during shaving, or some other form of traumatism, and which degenerates to form a deeply ulcerating and eventually fatal squamous cell carcinoma or malignant melanoma, is even yet all too common. By eradicating such benign lesions, especially when in locations subjected to the hazard of traumatism resulting in malignant change, the radiotherapist is actually working in the field of cancer prevention. It is our opinion that much can be done in the prevention of cancer by electrodesiccation or electrocoagulation of unhealthy tissue or lesions which sometimes precede cancer. Therefore, insofar as we can recognize and remove the unhealthy tissue which sometimes precedes the development of cancer, we can prevent cancer. Of course, no one can foretell just which of these lesions will develop into cancer, and consequently no one can ever decide to what extent or in how many cases we will have prevented cancer. It is true that a large percentage of such benign lesions may be completely cured by radiation therapy alone. However, by combining electrosurgery with irradiation the unhealthy tissue is actually removed before the irradiation is applied to its bed. Thus, the desired result is obtained with greater certainty. Electrocoagulation can be used to advantage in all such lesions which involve the skin or visible portions of the mucous membranes. This will include all warts, moles, hyperkeratoses, superficial

* Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

fissures or ulcers involving the skin, all localized patches of leukoplakia, fissures, sluggish ulcers, papillomata or polyps involving the mucous membrane of the mouth, the nose, the vagina, the rectum or the uterine cervix.

In the management of such cases one must always keep in mind the possibility that any one of these lesions may already have developed into cancer. If the lesion has shown recent increase in ulceration, crustation, degeneration, or new growth, the possibility of cancer must already be considered, and the entire lesion or a representative part of it should be removed for microscopic study followed immediately by complete destruction of the lesion. It is self-evident and a matter of ordinary experience that when any lesion is partially destroyed, there follows congestion, and the increased blood supply will naturally stimulate increased growth. It is our opinion that we have seen cancer stimulated and metastasis following such incomplete destruction and delay for microscopical report. For the same reasons, it is very bad practice to destroy any such lesions piecemeal. We have seen instances where such lesions have been partially destroyed three times a week for several weeks, and were followed by metastasis.

The technique for the destruction of these small superficial precancerous lesions of the skin is relatively simple, but we have seen instances where it has been badly done. Local anesthesia (novocaine) is suitable in nearly all instances. Each lesion must be anesthetized separately and sufficiently, otherwise the pain prevents complete destruction. The desiccating current should be used for these small lesions, and it should be a fine spark and done slowly so as to be sure to get all of the lesion but not to destroy healthy tissue unnecessarily. The destruction must always extend beyond the actual disease. It is our custom to curette away the desiccated or coagulated tissue. If such curetting reveals a bleeding base it indicates that the desiccation must be carried out more deeply. The scar even of these benign lesions can be improved by a local application of 80 to 100 per cent of an erythema dose of roentgen rays or radium. We are of the opinion that electrodesiccation increases the sensitivity of malignant cells to a greater degree than the production of such an effect in the normal cells, and that thus selective value of irradiation is enhanced, and Clark has concurred in this observation.

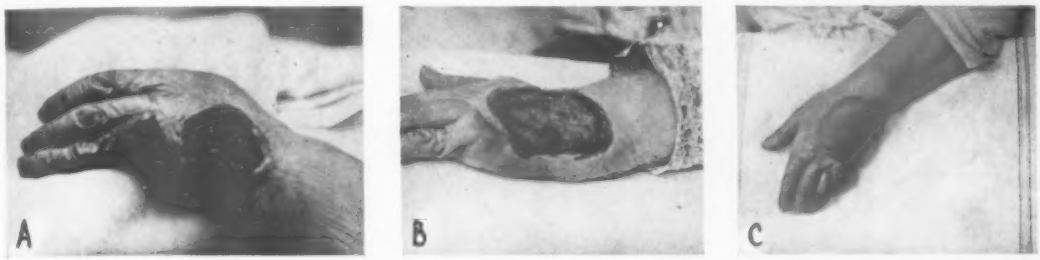


Fig. 1. *A*, epithelioma on the dorsum of the hand occurring in a scar following a burn, approximately twenty years previously. This was first destroyed by electrocoagulation. *B*, after healthy granulation tissue was formed a whole skin graft was applied by Dr. Stillwell Burns. *C*, electrocoagulation seems to be especially useful in these cases of squamous cell carcinoma developing on the basis of old scars.

These opinions regarding the treatment of lesions of the skin are based on experience obtained from numerous cases. During the period from 1910 to 1940 one of us (Pfahler) treated more than 1,100 patients by electrosurgery for the eradication of benign lesions of the skin. The actual number of lesions so eradicated greatly exceeds the number of patients and is in the neighborhood of 6,000 to 7,000. Many patients had

FIG. 2. *A*, patient, aged sixty, referred by Dr. E. G. Meter, December 2, 1920. Persistent epithelioma for seventeen years. Treated first by cancer paste, then removed in 1917, by electrocoagulation and again September, 1919. Treated by one of us (Pfahler) first with radium, then electrocoagulation. *B*, October 26, 1921. Healthy condition but deformed lip. *C*, condition of the lip January 14, 1928. The defect had been repaired by a plastic operation by Dr. Robert Ivy in April, 1922. Died of coronary disease December 31, 1933, thirteen years after our treatment.

multiple lesions and it has not been unusual to remove from 30 to 50 moles from the skin of a patient at one sitting; the largest number removed from one patient was 260. During the same period there were 1,580 patients with 1,976 epitheliomata of the skin treated by the combination of electrosurgery and irradiation. In almost all such cases, cancers of the skin, both basal cell and squamous cell, were treated by a combination of electrosurgery and irradiation. In only a very small percentage was electrosurgery omitted, and then only to avoid sacrifice of essential tissue or because of the location of the lesion, such as in the vicinity of an eyelid where it was desirable to avoid the production of a scar. That such combined treatment is effective is shown by the results. There have been 18 deaths due to cancer among 1,399 patients with epitheliomata of the skin who were treated up to the end of 1934. Thus we obtain a five year cure rate of 98.7 per cent.

LEUKOPLAKIA

In the destruction of leukoplakia on the alveolar process or the mandible it is advisable to carefully inject the anesthetic

FIG. 3. *A*, referred January 5, 1928, by Dr. Reeves of Bridgeton, N. J. He had had an epithelioma of the lip for nine months. He had been treated by electrodesiccation and radium irradiation. On the above date he had this extensive infiltration of the entire lip with extension down into the submental region on the left side, and into the submaxillary region as indicated on the photograph. *B*, on June 21, 1928, with a combination of irradiation and electrocoagulation he was free from any evidence of carcinoma and he has remained well to date. *C*, March 24, 1933, shows his condition after a plastic operation by Dr. Robert Ivy in which he transferred a whole pedicle skin graft from the anterior chest wall to the lip. Patient has remained well since and there has been a progressive improvement in his appearance.

just beneath the diseased area so as to separate it from the bone before destruction. If one destroys the periosteum with the high frequency current, death of bone will likely occur and generally an osteomyelitis will follow. We are convinced that this is the best method of dealing with leukoplakia, though any treatment with general medication, or the use of hormones or vitamins can very properly be used as an adjunct. It seems that the granulation tissue, which is formed with the violent reaction which follows such destruction, produces a healthier scar than any other method. One must be assured that the leukoplakia has not already degenerated into carcinoma, otherwise the congestion following this electrodesiccation will cause an extension of the carcinoma into deeper tissues. *We again emphasize that any doubtful tissue should be examined microscopically.*

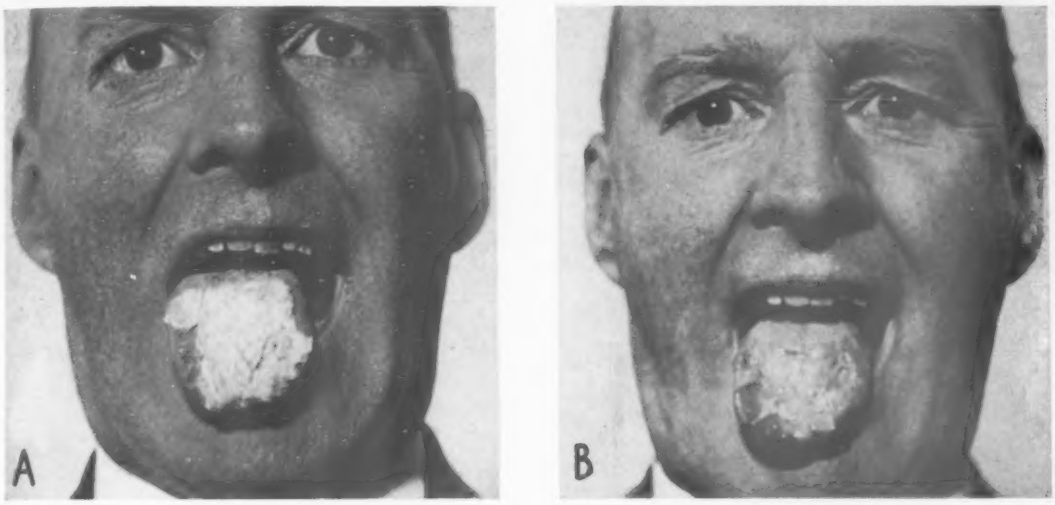


Fig. 4. *A*, shows an extensive leukoplakia referred on May 1, 1924, by Dr. R. R. Cummins, which has been developing during twenty years. He had smoked about 20 cigarettes a day for many years. The leukoplakia was about 3–5 mm. in thickness. The microscopic examination showed squamous cell carcinoma. The entire diseased area was destroyed and was followed by a total of 3,855 mg-hr. of radium, applied by surface application in divided doses, usually 100 mg. in 10 mg. radium units, filtered through the equivalent of 3 mm. of lead, and at 5 mm. distance. The radium packs were used externally with the radium filtered through 2 mm. of platinum, giving a total of 18,480 mg-hr. by surface application at 4 cm. distance. Preliminary to this irradiation the entire diseased area was destroyed by electrocoagulation. It is our experience that these leukoplakias do not yield well to local applications of radium and are better destroyed when possible by electrocoagulation. *B*, shows the condition of the tongue June 12, 1925. This patient died of heart disease on September 17, 1936, but his tongue had remained well.

CANCER OF THE LIP

We have found electrosurgery useful in most cases of cancer of the lip. In addition to its use for the destruction by the desiccation current of the precancerous lesions such as leukoplakia, scaliness, crusts, papillomata, fissures, and superficial ulcers, it is very effectual in the destruction of the early or small cancers (less than 1.5 cm. in diameter) after doing a biopsy. Generally, we surround the lesion with the desiccation current and then remove the entire lesion, if small, for microscopical study. We then destroy the base down to normal tissue. By practice the normal tissue can be recognized after curettement. It is a mistake not to remove all of the disease but one must aim to conserve as much tissue as possible for the sake of function and for cosmetic reasons. If these smaller lesions, 1–1.5 cm. in diameter, do not have much fibrous tis-

sue, good results can be obtained by using 6 to 8 erythema doses of relatively soft roentgen radiation localized and given within three to six days without destruction. This gives a good cosmetic result. Larger lesions (more than 1.5 cm. in diameter) are sometimes removed by electrosurgical dissection under local anesthesia and then successfully sutured. For sutures in these cases we prefer silk thread properly boiled.

There is another group of cases of cancer of the lip which may have been unsuccessfully treated by electrodesiccation, or irradiation, or some other method in which considerable scar tissue has formed. Such cases we have found do not yield well to further irradiation. In these cases, the remaining disease is best removed by electrosurgery. Generally such cases must have some plastic repair afterwards.

In all primary cases of cancer of the lip in which we have used electrosurgery the patients were given roentgen radiation, 1,800 to 2,400 r, over the lip and chin.

It must not be assumed that electrosurgery is used indiscriminately in the treatment of carcinoma of the lip. We consider it contraindicated when removal of the malignant tissue would produce an appreciable defect in the lip. Thus from 1910 to 1940, while 299 cases of cancer of the lip were treated by irradiation, only 236 of them received the combination of electrosurgery plus irradiation. Prior to 1935, 201 were treated by the combined method, among whom there were 14 deaths due to failure to control the cancer. Of the other 187 patients, 142 were living (and free from any indication of cancer) at the end of a five year period, while 25 had died of intercurrent disease (chiefly the usual diseases of old age) and 20 were not traceable. Omitting those who died due to intercurrent disease and those untraced, we obtain a five year survival rate of 91 per cent.

TABLE I

ANALYSIS OF CASES OF CANCER OF LIP TREATED BY COMBINATION OF ELECTROSURGERY AND IRRADIATION, 1911 THROUGH 1934

	Localized* Lesion	Extensive† Lesion	Glandular Involvement	Total
Well	114	16	12	142
Died of Cancer	1	7	6	14
	115	23	18	156
Survival at 5 years	99%	70%	67%	91%
Died of intercurrent disease	16	7	2	25
Not traced	14	4	2	20
Total	145	34	22	201

* Localized lesion—not more than 1.5 cm. in diameter, without glandular involvement.
† Extensive lesion—more than 1.5 cm. in diameter without glandular involvement.

It will be noted that one patient who arrived with a localized lesion died from cancer. The lesion was ½ inch in diameter and had been present for two years when he presented himself for treatment in 1919. Within two months all signs of cancer had disappeared and he remained apparently well for one and a half years. Then he returned with cervical node metastasis which proved to be beyond control and he died in 1923. With our present experience we believe that such an outcome might have been prevented by administering, at the outset of treatment, a greater dose of roentgen rays to the areas of lymphatic drainage.

CANCER OF THE TONGUE

In cases in which the leukoplakia shows

Fig. 5. *A*, shows an ulcerating adherent carcinoma involving the right breast occurring in a patient, aged seventy-nine, referred by Dr. Wm. E. Bray, on September 4, 1936. This carcinoma had been developing during more than five years. Axillary nodes were palpable. On September 17, under general anesthesia, one of us (Pfahler) removed the area of this right breast including a nodule from the axilla and then inserted into the axillary region five 10 mg. radium needles, and fourteen 10 mg. radium needles surrounding the edges of the wound. These needles were left in place four hours. Filtration was 0.4 mm. of monel metal. *B*, shows the condition of this wound on September 11, 1936. At this time, there was no palpable disease. *C*, shows this wound entirely healed, April 8, 1937. She has remained well since that date, and is now eighty-three. This case illustrates another field in which electrocoagulation can be combined to advantage with irradiation in carcinoma of the breast.

definite thickening or is in any way suspicious of having become cancerous, we remove the most suspicious area for microscopical study and then immediately destroy the remaining disease. Leukoplakia does not yield well to irradiation, though we believe that it is wise and helpful to apply surface radium after the destruction.

When definite clinical cancer of the tongue is present, we rarely begin with electrosurgery. Such cases are treated by irradiation with radium or the roentgen rays, or both. Sometimes, however, there remains a localized indurated area after one has given the normal tissue tolerance of irradiation. Then it may be practical to remove the local area by electrosurgery, and suture the wound. In such cases, it is advisable to ligate the lingual artery as a precautionary measure. There is an occasional case, however, in which a small lesion on the tongue is doubtfully malignant. In such a case it is a relatively simple matter to use the coagulating current to encircle the lesion, which may be removed bloodlessly with a small pair of scissors, or it can be removed by the electrosurgical "loop" electrode. Desiccation of the bed from which the lesion was removed completes the procedure, which is followed by intraoral irradiation (radium or roentgen rays) pending receipt of the microscopic report.

CANCER OF THE CERVIX

In this region electrosurgery has its greatest use in the prevention of cancer. It is probably the best method for the treatment of cervicitis, endocervicitis, lacerations, polyps and leukoplakia, and is ordinarily done by the gynecologists. In any doubtful case, which means nearly all cases, it is advisable to remove the most suspicious area for microscopic study. If the disease is superficial, electrodesiccation is very effectual. If the disease extends into the cervical canal, conization is best. If a polyp is present, it can be removed by the loop and the cutting current. We do not use electrosurgery in cancer of the cervix which can be diagnosed clinically.

CANCER OF THE RECTUM

In dealing with cancer in this region we have no rules. As in any other serious type of cancer, one must adapt the treatment to the individual case and the conditions which are present. In a few cases, however, when the disease is localized or is of the

scirrhous type, it is an advantage to destroy the local disease. This, of course, must be done under a general anesthetic. In such cases, we also make up a special applicator containing 150 to 200 mg. of radium in 2 mm. of platinum in felt and rubber and backed with lead, placed so as to irradiate only the involved portion of the rectum. The diameter of the applicator is from 3 to 4 cm. so that it can be inserted through the dilated sphincter; it is left in place from twenty-four to forty-eight hours. This combination method served well in the case of a man aged eighty-four, who in June, 1934, sought treatment for a polypoid adenocarcinoma, 10 cm. in length, reaching to within 3 cm. of the anus (Fig. 6). Under general anesthesia a colostomy was done by Dr. J. B. Carnett, and one of us (Pfahler) destroyed the tumor by means of electrocoagulation and inserted a tampon containing 150 mg. of radium which was left in place forty-four hours, giving a dose of 6,600 mg-hr. By September there was no sign of any carcinoma. In March, 1935, in spite of advice against it, the patient demanded closure of the colostomy. Therefore, after dilating the fibrous stricture in the rectum up to 2 cm. in caliber, the colostomy was closed in June, 1935. Subsequently the patient remained free from any recurrence of the rectal carcinoma. The stricture of the rectum did give him some trouble, chiefly leakage because of scar tissue in the sphincter, but he lived a much more active life than one would

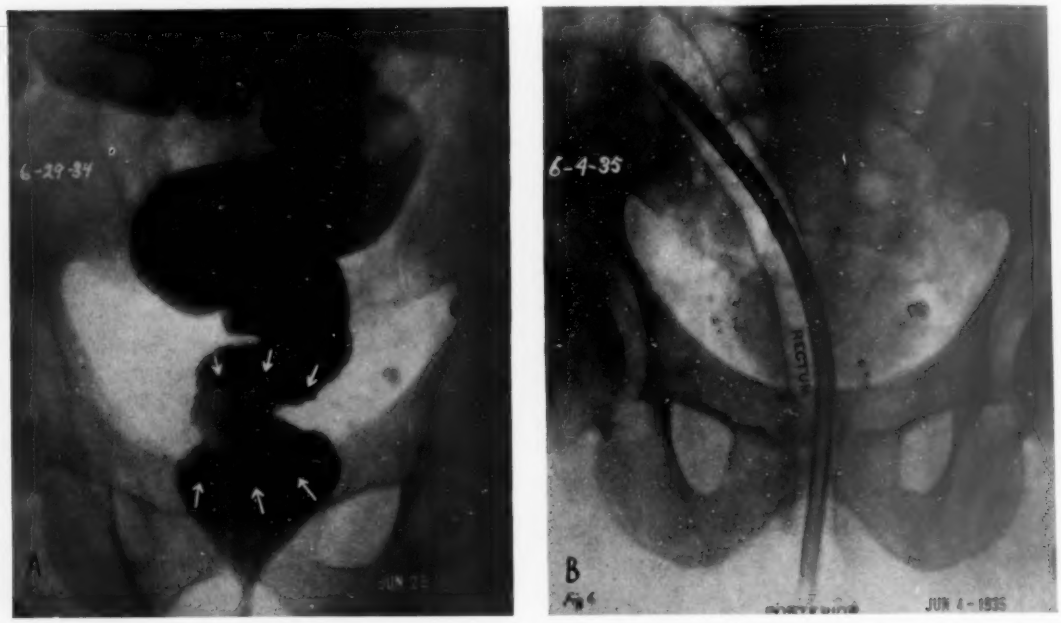


FIG. 6. *A*, carcinoma of the rectum, duration unknown, in a patient, aged eighty, referred by Dr. Samuel Salasin of Atlantic City on June 29, 1934. It will be observed that the carcinoma surrounds the rectum and involves an area approximately 5 cm. in length. Dr. J. B. Carnett did a colostomy. One of us (Pfahler) destroyed the diseased area in the rectum by electrocoagulation, and then 150 mg. of radium in the form of a tampon, using three 50 mg. tubes, filtered through 2 mm. of platinum, and with the radium 1 cm. distant from the tissue, the applicator being 4 cm. in diameter, was inserted into the rectum in the region of this tumor area and left in place for forty-four hours. He had four applications externally with radium packs, using 150 mg. of radium, applied over the lower abdomen and over the perineal region three times, the radium being at a distance of 4 cm., and each application was for a period of twenty-four hours. *B*, shows a smooth outline of the rectum on June 4, 1935, approximately one year later. The patient's rectum remained well but he died of carcinoma of the tongue with metastasis, April 9, 1938, or approximately four years after. He had always been a heavy smoker and we believe there was no connection between the carcinoma of the tongue and the carcinoma of the rectum.

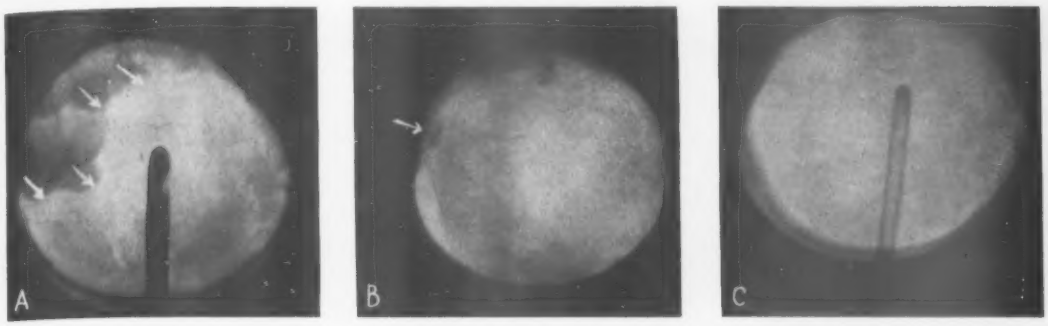


Fig. 7. Shows an infiltrating carcinoma of the bladder in a man, aged fifty-four, who was referred on May 8, 1933, by Dr. W. A. Mackinney. He had suffered from hematuria only two days preceding this diagnosis, made both by cystoscope and by pneumocystograms. *A*, shows an ulcerating infiltrating carcinoma involving an area 6 cm. in diameter, in the upper left quadrant of the bladder, located more anteriorly than posteriorly. It projected into the bladder lumen approximately 3 cm. *B*, pneumocystogram made January 8, 1934, showing a remnant of the tumor, about eight months after he had received approximately 4,000 r into the tumor area. At this stage at our request, Dr. Mackinney destroyed this remnant by electrocoagulation. It was then followed with further irradiation. *C*, shows a pneumocystogram with complete disappearance of this tumor, May 24, 1934, and this tumor has remained well during these six years. This illustrates how the bed of a tumor can be made more sensitive after it has apparently reached a resistant stage. It of course would be unwise to do extensive destruction after so much preliminary irradiation.

expect. In December, 1937, he reported with advanced carcinoma of the tongue associated with extensive metastasis which caused his death four months later, at which time he was still free from any recurrence of the rectal carcinoma.

Teperson, in a recent contribution, has fully discussed the treatment of carcinoma of the rectum by the combination of electrosurgery and irradiation, and the analysis of cases demonstrates the value of this method.

CANCER OF THE BLADDER

Electrocoagulation is also of use in the treatment of lesions of the bladder in selected cases. A man of fifty-four whose only symptom had been painless hematuria two days previously was referred in 1933. Cystoscopic examination by Dr. W. H. Mackinney, and pneumocystograms revealed a tumor of 6 cm. diameter on the left bladder wall with three small adjacent papillomata (Fig. 7, *A*). Roentgen therapy of 18,000 r to the skin delivered an estimated 6,500 r to the tumor and in four months the tumor had become reduced to 10 per cent of its original size (Fig. 7, *B*). At this stage, Dr. Mackinney destroyed the residual tumor tissue by electrocoagulation through the cystoscope. Since that time the patient has lived actively, free from signs or symptoms of cancer (Fig. 7, *C*).

This exemplifies the type of case in which the combination of those methods is suitable. Here, because the tumor was very large, initial electrocoagulation was out of the question. It could not be carried out until the tumor had been greatly reduced in size by irradiation. However there are cases in which the lesion of the bladder may be encountered at an early stage and still be very small. In such cases the method of choice would be first to electrocoagulate and then to follow immediately with roentgen irradiation.

SUMMARY AND CONCLUSIONS

1. We have reviewed very briefly our experiences with electrosurgery (electrodesiccation, electrocoagulation) in conjunction with or as an adjunct to irradiation during the period from 1910 to 1940. This comprises a record of more than 2,500 cases.

2. Electrosurgery has been proved of definite value both in the prevention and in the cure of cancer.

3. Failures from irradiation can often be

transformed into success by this combination.

4. In cancer of the skin, there have been 100 per cent five year recoveries in patients treated before the deeper structures were involved.

5. Counting all cases of cancer of the skin, including those which have involved deeper tissues (fascia, muscle, cartilage, mucous membrane or bone), the results still show 98.7 per cent five year recoveries.

6. Small (1.5 cm. in diameter) cancers of the lip without glandular involvement have shown 99 per cent five year recoveries.

7. The method has been found of definite value as an adjunct in the treatment of cancer of the mouth, tongue, cervix, rectum and bladder.

REFERENCES

1. CLARK, W. L. Electrosurgical Methods. Principles and Practice of Physical Therapy. Edited by Mock, Harry E., Pemberton, R., and Coulter, John S. Vol. 2, Chap. 20, pp. 65. W. F. Prior Co., Hagerstown, Md.
2. PFAHLER, G. E., and VASTINE, J. H. Treatment of epithelioma of the skin. *Radiology*, 1934, *23*, 542–547.
3. TEPERSON, H. I. Treatment of carcinoma of the rectum by electrocoagulation and radiation, in selected cases. *Radiology*, 1940, *34*, 610–617.

DISCUSSION

DR. THOMAS J. ANGLEM, Boston. Dr. Pfahler in his very interesting paper has appropriately called attention to the advantages at times of using electrocoagulation in combination with radiation therapy. I have been very much interested in the wide scope of the indications which Dr. Pfahler finds for the use of this combined method.

We have used the combined method of treatment to a considerable extent here, but on indications much less broad than those of Dr. Pfahler's, and limited in general to three main categories. The first of these is illustrated by Dr. Pfahler's case of carcinoma of the bladder, which you have just seen demonstrated, and may be expressed in general terms as that group of cases in which, after a full course of roentgen therapy given up to the limit of the patient's tolerance, there still remains residual tumor, which is technically removable by electrosurgery.

We have found this method of treatment particularly applicable in intraoral cancer and in certain advanced cancers of the skin, particularly those in the region of the ear, the external auditory meatus, and the dense tissue overlying the mastoid region—areas in which the usual alternative procedure of wide surgical removal and plastic repair is not feasible because of the almost invariably high degree of fixation which occurs in these areas, and the density and inelasticity of the tissues.

The preliminary irradiation in these cases brings about a marked shrinkage of the disease, following which the volume of tissue which must be removed by electrosurgery is very much less than when electrosurgery is chosen as the primary form of treatment. Nevertheless these operative procedures are often of considerable magnitude, and are not to be undertaken lightly.

The second method of treatment which I have used to advantage is that developed in the Memorial Hospital in New York—the so-called method of overdosage with gold seeds followed by electrosurgical removal. This method of treatment is applicable particularly in advanced carcinomas of the tongue, which are ulcerated and associated with considerable secondary infection and necrosis. Gold seeds are implanted interstitially, and the desired dosage is so calculated as to be delivered within a period of four or five days, after which time the condemned, necrotic and infected tissue, in which the seeds have been buried, is removed by electrocautery. This results in the elimination of a long period of sloughing of the infected tumor, and yet a lethal dose of radiation is delivered to the surrounding portions of the tongue, which takes care of any residual cells which may have been left behind.

The third method which I have used frequently and found extremely useful is applicable in certain carcinomas of the skin and mucous membrane which are not deeply infiltrating, but are growing more in a proliferative fashion, forming elevated tumor masses above the skin or mucous membrane surface. The method is used particularly in the case of tumors elevated 7, 8 or 10 millimeters, or more, above the surface of origin. We convert the lesion into a flat one by simple cautery removal of the redundant portion of the lesion, and then proceed with subsequent irradiation of the base. The advantages of this form of treatment are

obvious. The bulk of the tumor is removed in one stroke, and the remaining small amount of disease can be destroyed by much smaller amounts of radiation than would have been required otherwise.

Dr. Pfahler attempts to destroy the lesion completely before following through with the radiation therapy, and is accustomed to employ it in even the most superficial skin carcinoma. The rational basis for this form of treatment, as I have described it, continues to apply, but with gradually diminishing force for lesions of lesser and lesser thickness or degree of infiltration, and at just what point it no longer becomes practicable to employ the combined method I think is a matter that is open for debate.

Practically we have not found it necessary or desirable to use the combined method in the average type of skin cancer, but have preferred to use surgical excision or destruction by electrocautery or radiation therapy, depending on the indications in each individual case.

There is this to be said for Dr. Pfahler's double attack—the successful outcome in any individual case is dependent on complete destruction of the disease by whatever method is employed. By using two methods, and using both in full dosage, a certain margin of safety is granted, and where one method is applied in insufficient dosage to bring about complete destruction of the tumor, a clinical cure may still result due to the effect of the second component of the treatment.

In any event, Dr. Pfahler's figures are extremely impressive, and there can be no doubt that this method of treatment in his hands is extremely effective.

I should like to say one more word, briefly, about the treatment of premalignant moles. It has been my experience that a substantial number of the cases which I have seen have been recurrent after ill-advised electrodesiccation or electrocoagulation, and this experience has not been unique. In the large series of cases reported by Dr. Frank Adair and Dr. Ernest Daland the same observation has been made. It is my opinion that no case of mole in which one has any reason to suspect that it is possibly premalignant because of deep pigmentation, blue-black color, or by reason of recent change in character, should be treated by electrodesiccation in situ, but rather by complete surgical excision, using the diathermy knife if you wish, but with a large margin of normal skin around it, and a generous layer of subcutaneous tissue.

Dr. Pfahler (closing). I didn't intend to say anything, but the last sentence, that finishing sentence, I must answer. First of all, I say most emphatically that any case of pigmented mole —I hope you are all hearing me—*any case of pigmented mole in which there is any possibility of cancer at all should be removed by electrosurgery or electrical destruction and not by excision.* The essential thing is that it must be thoroughly done. I, too, have seen recurrences, but they were recurrences after incomplete destruction and incomplete removal by surgery, and particularly I want to emphasize that it is not the type of case in which you want to take the top off and then depend upon irradiation to cure. I hope I have made myself sufficiently emphatic on that point. I think that is more important than anything else I told you. I have never had a recurrence after destruction of a malignant melanoma. I have had metastases, but I am reasonably sure they were present before I destroyed the local lesion.

TUBERCULOUS TRACHEOBRONCHITIS

ROENTGENOGRAPHIC APPEARANCE

By WALDO R. OECHSLI, M.D.
Olive View Sanatorium
OLIVE VIEW, CALIFORNIA

IN 1836, Louis[16] made a careful pathological description of tuberculosis of the trachea, which he found on postmortem examination in 6 out of 31 cases of pulmonary tuberculosis. Despite early knowledge of this pathological condition, recognition of the clinical aspects and of the importance of the rôle played by the complication has come about only in the last decade following the work of Eloesser,[10,11] Coryllos,[7,8] and others. Regarding the direct roentgenographic appearance of the condition little has been written. With two exceptions, the only reference in the American literature has been to indirect signs, such as atelectasis and "balloon" or "tennis ball" cavities. Holcomb and Weber,[13] referring to dense shadowing between a pulmonary cavity and the hilum, say, "The stem of stem cavities may be nothing else than the bronchus filled with fibrotic tissue." Coryllos felt that shadowing between the cavity and the hilum often represented a thickened bronchus but did not describe what he considered the characteristic nature of this finding.

Only within recent weeks, there has come to my attention the fact that Ameuille and Levesque,[2] as early as 1923, described the roentgen findings of this condition, using the term "draining bronchus of tuberculous cavities." Their description is practically identical to that which I have used in the following presentation of the direct roentgenological evidence of tuberculous tracheobronchitis, without knowledge of this earlier work. This was confirmed by Wolf[26] and Raabe.[20] Ameuille, Delhomme and Raust[1] later made a careful anatomic-pathologic study based on 27 autopsy cases. Otherwise these findings appear to have received little attention in the European literature and none in this country, despite the interest aroused by wider use of the bronchoscopic examination in tuberculous patients.

On the basis of a study of several hundred proved cases of tracheobronchitis due to tuberculosis and a correlation with bronchoscopic and autopsy findings, the roentgenographic appearances described below are considered characteristic of this pathological entity. These findings were presented as an exhibit at the National Tuberculosis Association convention at Los Angeles, California, in June, 1938. Peirce and Curtzwiler[19] have lately described the roentgen pathology of this condition, presenting 6 cases chosen out of a total of 40 cases of tuberculous tracheobronchitis which they had studied, confirming the roentgenographic signs described in our exhibit. They note the following roentgenographic changes: "atelectasis, spontaneous intermittent atelectasis, extent of roentgen pathology not compatible with clinical course, degree of collapse greater than expected from evident lesion, sudden, increased atelectasis with collapse therapy, visible changes in bronchi and tennis ball cavity."

Preliminary to the discussion of the roentgenographic evidence of tuberculous tracheobronchitis, it seems advisable to review the roentgenographic appearance of the normal lung, in order to avoid perpetuating a misconception that still exists to some extent regarding the significance and cause of the images cast on the film by the normal lung and commonly known as "lung markings" and occasionally referred to as "thickening of the trunks," "beading," etc.

The classical work along this line was performed in 1911 by Dunham, Boardman and Wolman.[9] In a careful and thorough experiment, a human lung was removed

from a cadaver soon after death and roentgenographed. A bronchus with its associated vessels was selected and by careful dissection a vein was removed and laid across another part of the lung. A second roentgenogram showed this excised vein clearly and the original lung marking was diminished in density. The artery was then dissected out with further decrease in density of the original shadow. Finally, the bronchus was dissected out, after which nothing of the original shadow remained in the roentgenogram. Their conclusions, which still appear valid after twenty-nine years, were that "these shadows seen in the lung fields are due to the blood vessels with their contained blood and to the walls of the bronchi. The blood vessels with their contained blood must cast more shadow than do the walls of the smaller bronchi with their contained air."

Having thus very clearly and definitively demonstrated the cause of lung markings in the normal lung, Dunham later stated that early tuberculosis is characterized by changes in which "the fine linear markings appear broader, denser and less regular in outline, frequently their course is studded, sometimes almost to obliteration of the lines. We can no longer trace them as radiations but find them broken in continuity and reaching to or near the periphery." Other observers, while accepting the truth of Dunham's original work on the cause of lung markings, have cautioned against confusing these lung markings with pathological conditions in the parenchyma. Miller,[18] studying the lung of the pig and of the dog, issued this warning, "In reading X-ray plates, care should be exercised not to mistake these linear markings for densities produced by pathological changes." McPhedran[17] opposes the conception also in these words, "Sometime ago it was common and even today it is not unknown for the prominence of the trunks ascending into the apex to be ascribed to tuberculosis. The description is thickening and beading of the apical trunks and the diagnosis peribronchial tuberculosis or tuberculosis spreading out from the hilum. For such a diagnosis there is no pathological basis . . . the so-called thickened and beaded bronchus is merely a normal but prominent blood vessel, whose smooth, sharp contour, moreover, and gradually decreasing caliber give no suggestion of the irregular deposition of density about it that would be the result of an infiltration."

It is entirely true that lung markings have too often and too long been confused with shadows caused by parenchymal changes. Furthermore, there has been a great deal of confusion regarding the relation of increased density and prominence of pulmonary markings and pathological involvement of the bronchi. Quite recently, Andrus,[4] referring to the roentgen diagnosis of bronchiectasis, stated that these increased pulmonary markings "may be observed in two classes of disease, vascular and infectious processes. In general, if there are no radiographic or clinical clues to suggest that such a change is vascular in origin, it may be taken to represent probably an infectious injury." It is granted that there may be an increase in density of pulmonary markings in bronchiectasis but it is my feeling that these findings which he terms "mural shadows" probably have as their origin an increased vascular congestion incidental to the infection and that a diagnosis of mural thickening of the bronchi should have a more solid foundation than generalized or localized increase in density of pulmonary markings or density of hilar shadows.

Most tuberculous involvement of the bronchi or trachea follows cavity formation in the lung. Probably the chief method of origin is by direct extension from the pyogenic membrane of the cavity along the bronchus. Implantation also occurs at points farther away from the cavity with the intervening bronchial mucosa uninvolved. Another method of origin is by way of extension from contiguous lesions in the parenchyma or in tracheobronchial lymph nodes. The resulting lesions, regardless of origin, may take a number of forms.

In a highly sensitized individual, there may be a diffuse, allergic, inflammatory change with congestion and edema of the mucous membrane, resulting possibly from mere passage of bacilli-laden sputum over the mucosa. This type of involvement probably occurs relatively early, affects a larger number of bronchi and clears up more readily than other forms. Of more serious import is actual invasion of the mucosal or submucosal layers of the bronchi or trachea by tubercle bacilli, leading to tubercle formation with nodulation and even ulceration. At times, during the healing process, or in the attempt to heal, fibrosis occurs with narrowing and even complete stenosis.

Incidence depends on the type of patients studied. Hawkins[12] found positive bronchoscopic evidence of tuberculous tracheobronchitis in 25 per cent but this was in patients selected because of suspicion that the complication existed. Shipman[21] reports finding 10 per cent in autopsy material at the University of California. Bugher, Littig and Culp[6] report a higher incidence. Among 122 cases of pulmonary tuberculosis coming to autopsy, they found tuberculous involvement of the trachea in 20.5 per cent and of the bronchi in 33.6 per cent. Warren, Hammond and Tuttle,[24] in a routine series of bronchoscopic examinations on pre-thoracoplasty cases, found bronchial ulceration in 13.3 per cent.

The roentgen findings in tuberculous tracheobronchitis are of two types, indirect and direct. Indirect evidence consists of the roentgen findings caused by conditions secondary to bronchial pathology which lead us to infer that tuberculous involvement of an air passage exists. Direct evidence consists of the roentgen findings resulting from pathological changes in the air passages themselves, rather than some remote effect of such a lesion.

INDIRECT EVIDENCE

1. *Localized Emphysema.* Westermark[25] has recently described an early roentgenographic sign of bronchostenosis consisting of a localized area of emphysema. He considers this condition due to partial stenosis of the regional bronchus with a check-valve mechanism hindering passage of air out of this part of the lung on expiration. The more or less wedge-shaped area of emphysema is outlined by convex borders and is described as occurring more often in the upper lobes in contradistinction to compensatory emphysema. It is often followed in later examinations by atelectasis in exactly the same part of the lung. This has been observed in a very few cases here with visible evidence of bronchial thickening, although the subsequent development of atelectasis has not been observed as yet.

2. *Atelectasis.* Atelectasis of a lobe or a lung in pulmonary tuberculosis is caused primarily by obstruction to the passage of air through the bronchus supplying that lobe or lung. This obstruction, sometimes caused by tenacious sputum, blood, pressure from an enlarged gland or a foreign body, more often results from intrinsic tuberculous involvement of a bronchus. Depending on the location of such an obstructive lesion, one sees atelectasis of a lobe or entire lung, characterized by opacity, diminished volume, homolateral displacement of the mediastinum, heightening of the hemidiaphragm and narrowing of the intercostal spaces of the involved half of the thorax. The direction and extent of displacement may be affected considerably by previous fixation by pleural thickening. In serial examinations, these changes may occur suddenly or there may be a gradual decrease in volume with diminishing aeration, the bronchi in the involved lobe or lung coming to lie closer together with decreased aeration of the parenchyma between the tortuous, distorted branches. This partial atelectasis of a lobe often eventuates in complete atelectasis.

Whether complete atelectasis of part of a lobe can occur is a moot question and is denied by Van Allen and Lindskog.[23] Their contention is based on inability to produce atelectasis of less than an entire lobe experimentally in animals, which they attribute to passage of air through anatomic connections between alveoli. However, the presence of an inflammatory process in the

alveoli, as in pulmonary tuberculosis, might presumably close or obliterate these pores, preventing collateral passage of air through them and thus allow atelectasis of part of a lobe to develop. A few observations here indicate that atelectasis of part of a lobe has occurred in patients.

3. *Balloon or Tennis Ball Cavities.* The presence of round or smoothly oval cavities, frequently with a fluid level, and presenting an appearance of being under tension and distended (Fig. 1), should suggest the possibility and even probability of some degree of tuberculous involvement of the bronchiole or bronchus leading from such a cavity, with narrowing of its lumen. This narrowing may be too far distal to be visualized bronchoscopically. Observation has been made that normally the caliber of a bronchial lumen is 100 per cent greater during inspiration than during expiration.[14] Coryllos applied this observation to the tuberculous cavity to explain positive pressure which he had found within cavities. According to this theory, partial stenosis, such as may be caused by mucosal or submucosal swelling or thickening, may cause sufficient obstruction of the lumen of the bronchus proximal to the cavity that, during expiration, passage of air out of the cavity will be hindered, while the increased caliber, during inspiration, allows air to enter the cavity freely. Increased pressures would thus be built up within the cavity, accounting for their round or oval shape and for their failure to close.

Other factors undoubtedly enter into the failure of cavities to close but positive pressure has been noted in some cavities here and must be considered a real factor. On needling cavities, Kupka[15] has found pressures in some cavities varying from +2 to +30 cm. of water. In one instance, a pressure of +4 went to +30 after a coughing spell and remained so for a number of respirations, coming down slowly after a number of deep respirations to +4 again.

The above quoted theory of Coryllos might therefore be amplified, in the light of the above experience, by the inclusion of what Andrus[3] has termed "abnormal expiration," resulting from "unusual obstruction to the outflow of gas; unusual force applied to produce the outflow of gas; or . . . a combination of the two." During a coughing spell, positive pressure is suddenly built up in the thorax. In the case cited above, this high pressure must have been transmitted to the interior of the cavity, not so much by compression of the cavity walls as by the introduction of more air into the cavity during the expiratory phase of cough, as indicated by the persistence of high pressure through a number of succeeding respirations. If the communicat-

FIG. 1. C.V. Balloon cavities in the upper and lower lobes (indicated by arrows). Cavities uninfluenced by mechanically good collapse. Only apical adhesions seen, yet chief collapse is over middle portion of lung, draping around the distended cavities. Bronchoscopy showed tuberculous ulceration of posterolateral wall of main bronchus and stenosis of upper lobe bronchus on this side, with fiery red granulations. Cavities persisted until after completion of seven rib thoracoplasty with no change other than slight flattening and then closed suddenly with conversion of a grossly positive sputum.

FIG. 2. K.W. Atelectasis involving entire lung. Potter-Bucky film shows encroachment on the lumen of main bronchus with almost complete stenosis (indicated by arrows). Confirmed by bronchoscopy. Distal cavitation and bronchiectasis.

ing bronchus were stenosed to a greater degree than in the above case, air might still be forced into the cavity during cough but not leave the cavity so readily, allowing persistence of even higher pressure than the 4 cm. of water noted in this case. With complete stenosis, even cough might not be sufficient to force air into the cavity and with absorption of the air in the cavity, the latter would close.

4. *Sudden Disappearance of Cavity.* It happens too often to be dismissed as coincidence that cavities under pneumothorax collapse, after remaining for weeks or months without change, instead of closing gradually will suddenly disappear without any change in therapeutic management. Occasionally, we see a cavity which is unaffected by pneumothorax close promptly after pneumothorax is abandoned.[22] Such occurrences would seem best explained by complete stenosis of the bronchus draining the cavity, converting a partially blocked cavity into a completely blocked one.[21] This was confirmed experimentally in a human being by temporary obstruction of a bronchus by a rubber balloon introduced through a bronchoscope.[5] The induced pneumothorax, which had been free from adhesions but not selective, became so at once; the cavities closed promptly and remained closed.

5. *Re-opening of a Cavity.* It is often difficult to be certain, when a cavity has reappeared, that it is the same cavity previously present in a given area. Even if careful localization shows the cavity to be in the same part of the lung, it is possible for tuberculous infiltration to have broken down to form a new cavity. However, if one can be confident that a cavity recently closed has re-opened, this occurrence would suggest that the original cavity had become completely blocked for a time, the air absorbed and, before organic healing could take place, some change in the condition of the draining bronchus allowed it to become filled with air again.

FIG. 3. K.W. Same patient after thoracoplasty. Stenosis still present and demonstrated by lipiodol. Distal bronchiectasis.

6. *Unexplained Spread of Infiltration.* A bronchogenic spread of infiltration, in the absence of demonstrable cavitation or hemorrhage, might well be caused by aspiration of purulent material containing tubercle bacilli from an ulcer in the trachea or one of the bronchi. Probably some of the so-called "re-activations" occur in this way as a result of spread from a tracheobronchitis which had persisted unhealed for a period of time after the cavities or other parenchymal lesions had become healed.

DIRECT EVIDENCE

1. *Encroachment on Lumen of a Bronchus.* This evidence refers chiefly to the larger bronchi where gross changes in the shape of the lumen can be visualized to better advantage than in smaller branches. With lesser degrees of thickening and stenosis, the normal tapering shadow representing the lumen is narrowed, sometimes irregularly, and there may be distal dilatations (Fig. 2). In complete stenosis, there is a sharply tapering conical shadow which ends at the point where stenosis is present. In some cases, where granulations fill the bronchus, the shadow of the bronchial lumen ends abruptly, sometimes with slight proximal dilatation. Confusing shadows often overlie the bronchus making clear visualization difficult or impossible. The use of a Lysholm or Potter-Bucky grid or laminagraph is advisable.

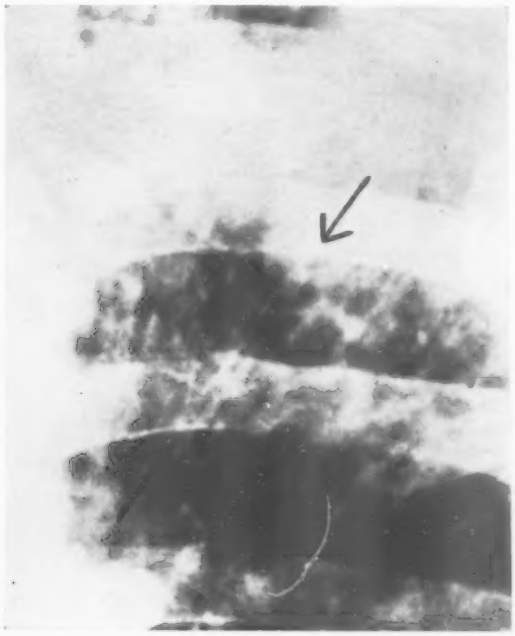


FIG. 4. J.W.P. Double, white line (indicated by arrows) characteristic of thickening of bronchial walls, extending from hilum toward a cavity in upper lobe. Bronchoscopy showed no pathological condition on first examination but later showed slight submucosal nodulation in upper lobe bronchus of same side.

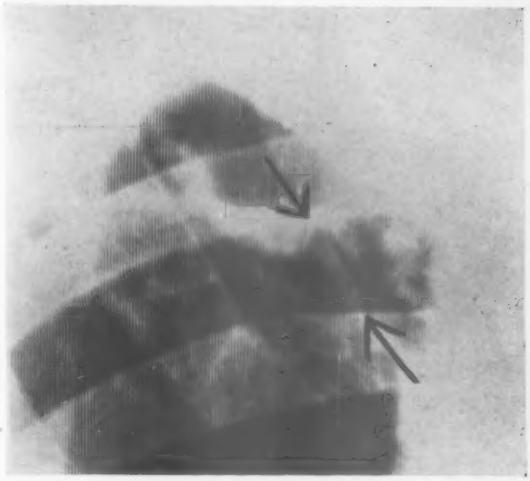


FIG. 5. R.H.M. Rather heavy double, white lines indicating more advanced bronchial thickening with a very narrow lumen.

2. *Encroachment on Lumen Outlined by Contrast Medium.* Where there is insufficient contrast or too many confusing shadows to secure clear visualization, iodized oil will outline the air passages satisfactorily (Fig. 3). Narrowing of smaller branches beyond the sight of the bronchoscopist may also be visualized in this way, though the factor of incomplete filling must be watched for.

3. *Thickening of the Bronchial Wall.* While a normal bronchus contributes to a slight extent to the lung markings seen on the film, it rarely casts a shadow which can be differentiated from that of the associated blood vessels or can be recognized as the shadow of a bronchus per se, except in the case of the main bronchi and their larger branches. When a disease condition such as tuberculous inflammation causes an increase in thickness of the walls of the smaller bronchi, there is sufficient density

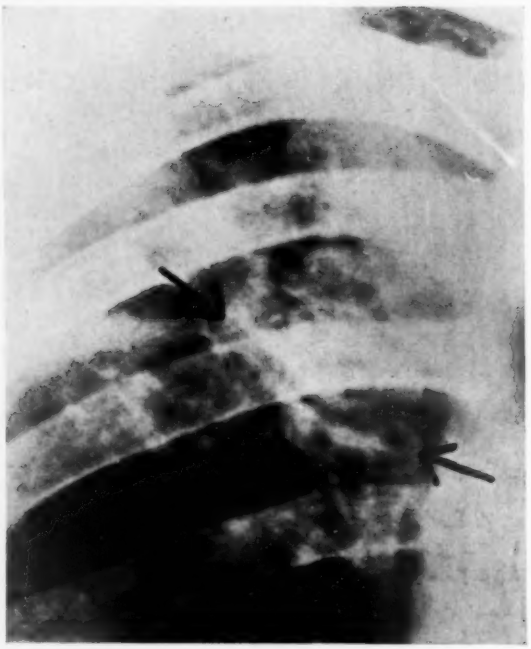


Fig. 6. J.A.S. Heavy double white lines extending out toward a cavity below the clavicle. Bronchoscopy showed ulceration of the upper lobe bronchus, on the same side, with stenosis.

to cast a well defined shadow on the film, under certain favorable conditions. If the thickening is not sufficient to cause complete stenosis of the bronchus, the walls of the thickened bronchus, shown in profile, are projected onto the film as two white lines separated from each other by a dark shadow representing the lumen of the bronchus (Figs. 4–8). The width of this dark shadow corresponds roughly to the width of the lumen expected in the part of the lung being examined, wider near the hilum and narrower toward the periphery. If there is encroachment on the lumen by the pathological process, it will be narrower than normally (Fig. 5). There is some variation in the thickness of the white lines representing the thickened walls of the bronchi. In early cases, these lines are quite sharply defined and thin (Fig. 7) but in cases with more advanced involvement, the lines may be several millimeters thick (Fig. 6).

These double, white lines are usually so fine that conditions must be favorable for projection onto the film with sufficient clarity to permit positive identification. There is such a wealth of detail in the average chest film, especially in far advanced or long standing pulmonary tuberculosis, that one may easily be confused by shadows which simulate bronchial thickening but which may be caused by a normal condition or some other pathological condition. Two blood vessels running parallel might be a confusing factor but blood vessels usually cast a wider shadow and diverge and diminish in width toward the periphery of the lung. Fine lines cast by fibrotic strands or an interlobar fissure can be confusing but very careful study of these lines will usually show that they diverge or cross each other or extend entirely out to the pleura.

These double white lines, cast by thickened bronchial walls, cannot be visualized on the film unless there is the double contrast afforded by air in the lumen of the

Fig. 7. C.L. Partial collapse of lung by pneumothorax, which had resulted in closing of a balloon cavity. There remains a V-shaped double line indicating localized thickening of a branched bronchus. Bronchoscopy showed submucosal nodular thickening in the main bronchus on the same side with fiery red granulations stenosing the lumen to 5 mm. diameter.

bronchus and air in the surrounding parenchyma. Conditions such as atelectasis, pleural effusion, consolidation, dense infiltration destroy the necessary contrast. Complete stenosis of the bronchus or filling of the lumen with sputum or blood would also destroy the contrast. The blood vessel associated with the bronchus often overlies the bronchus, obscuring the contour of the bronchial wall. Mere visualization of the bronchial lumen, if it is of normal contour and outline, is not sufficient to justify a diagnosis of thickening of the walls of the bronchus (Fig. 1).

Evidence of bronchial thickening is most often visualized fairly well out in the lung, proximal to a cavity, though it may extend entirely to the major bronchi at the hilum. Other branches, tributary to this bronchus, are quite often uninvolved. Occasionally, it is seen between a dense lesion, such as an area of caseation, and the hilum. Usually, the number of bronchi involved is limited to one to three. In a patient with recent, active infiltration, presumably with a high state of allergy, slight thickening of a larger number of branches in the infiltrated parts of the lung is often seen, while a patient with more long standing, chronic involvement will have a more localized bronchial involvement, especially if cavitation is present. Similarly, there is usually regression of these more widespread findings in the same patient as the disease process or the patient's reaction to it quiets down.

Study of the bronchoscopic findings in a large number of patients has shown good correlation with this sign. In most cases, bronchoscopy showed the lobar bronchus to be involved when the roentgenogram indicated the presence of bronchial thickening in that lobe. In some cases, positive from the roentgen standpoint, no pathological condition was seen bronchoscopically, probably due to the fact that the disease process had not at that time extended far enough proximally in the respiratory tract to be seen bronchoscopically. In fact, 12 of these patients, negative at the first bronchoscopy, were later seen to have definite tuberculous involvement of some portion of the major bronchi. Eleven of these 12 cases had presented direct or indirect roentgen evidence of tuberculous tracheobronchitis at the time of the first bronchoscopy. In most of them, the bronchoscopic evidence of advancing tracheobronchitis was paralleled by increasing roentgen evidence of the condition in succeeding films.

Fig. 8. C.F.W. Double white line indicating thickening of the walls of a bronchus extending out toward a large balloon cavity with a fluid level. Several bronchoscopic examinations showed submucosal nodulation, ulceration and progressive stenosis of the main bronchus on the same side.

Body Section Roentgenography

Somewhat in contrast to the value which I have come to attach to this new diagnostic method in the study of cavity and caseous lesions, the findings in tracheobronchitis have been a little disappointing. In a fair number of cases examined by this method, stenotic lesions in the larger bronchi have been shown with slightly greater clarity than in conventional films. The character of the pathological changes in the smaller branches of the bronchi is shown in a much smaller proportion of cases. Probably the chief reason for this is that in order that a given section of a bronchus may be faithfully recorded on the film, it must lie in the plane of sharp definition, rather than pass

through that plane at an angle. In most parts of the lung, the latter condition obtains and the bronchus will appear to terminate at the point where it leaves the plane of sharp definition. By studying the next section, the bronchus may be picked up again as it passes through that plane. Little can be judged under these conditions and it is therefore only occasionally, where the involved portion of a bronchus lies within the plane of sharp definition, that we can profit by this diagnostic method.

SUMMARY

Tuberculous tracheobronchitis is a complication of pulmonary tuberculosis occurring in probably an average of 15 per cent of all far advanced cases. It involves chiefly the part of the respiratory tract leading from cavities to the major bronchi and trachea, apparently always progressing in this direction. Based on a study of several hundred proved cases, the indirect and direct roentgenographic evidence of the condition is described, differentiating these findings from normal "lung markings" and from a finding that has been too loosely designated in earlier writings as "bronchial thickening" or "thickening and beading of the trunks." Some of the clinical implications have been briefly touched upon, indicating the far-reaching effect this complication has upon the evolution of pulmonary tuberculosis.

REFERENCES

1. AMEUILLE, P., DELHOMME, and RAUST, J. La bronche de drainage des cavernes tuberculeuses (étude anatomique). *Ann. d'anat. path.*, 1936, *13*, 849–855.
2. AMEUILLE and LEVESQUE. La bronche de drainage des cavernes tuberculeuses. *Bull. et mém. Soc. méd. d. hôp. de Par.*, 1923, *47*, 612–614.
3. ANDRUS, P. M. Mechanics of respiration. *Am. Rev. Tuberc.*, 1936, *33*, 139–164.
4. ANDRUS, P. M. Chronic nonspecific pulmonary disease. I. The radiographic diagnosis of bronchiectasis. *Am. Rev. Tuberc.*, 1940, *41*, 87–98.
5. BROOKS, W. D. W. An ancillary method in treatment of pulmonary tuberculosis. *Brit. J. Tuberc.*, 1938, *32*, 14–19.
6 BUGHER, J. C., LITTIG, J., and CULP, J. Tuberculous tracheobronchitis; its pathogenesis. *Am. J. M. Sc.*, 1937, *193*, 515–525.
7. CORYLLOS, P. Importance of atelectasis in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 1933, *28*, 1–26.
8. CORYLLOS, P. Mechanics and biology of tuberculous cavities. *Am. Rev. Tuberc.*, 1936, *33*, 639–660.
9. DUNHAM, H. K., BOARDMAN, W. W., and WOLMAN, S. Stereoscopic x-ray examination of the chest with especial reference to diagnosis of pulmonary tuberculosis. *Johns Hopkins Hosp. Bull.*, 1911, *22*, 229–238.
10. ELOESSER, L. Bronchial stenosis. *J. Thoracic Surg.*, 1932, *1*, 373.
11. ELOESSER, L. Bronchial stenosis in pulmonary tuberculosis. *Am. Rev. Tuberc.*, 1934, *30*, 123–180.
12. HAWKINS, J. L. H., JR. Tuberculous tracheobronchitis. *Am. Rev. Tuberc.*, 1939, *39*, 46–56.
13. HOLCOMB, F. W., and WEBER, G. W. Atelectasis and disappearance of cavities. *Am. Rev. Tuberc.*, 1934, *30*, 299–306.
14. HUDSON, W. A., and JARRE, H. A. Cin-ex camera studies of tracheo-bronchial tree. *Grace Hosp. Bull.*, 1929, *13*, 15–34.
15. KUPKA, E. Personal communication.
16. LOUIS, P.-C.-A. Pathological Researches on Phthisis. Hilliard, Gray & Co., Boston, 1836, p. 43.
17. MCPHEDRAN, F. M. Roentgenogram in early tuberculosis in adults. *U. S. Nav. M. Bull.*, 1932, *30*, 91–104.
18. MILLER, W. S. Stereoroentgenograms of injected lung as an aid in study of lung architecture. *Bull. Johns Hopkins Hosp.*, 1919, *30*, 34.
19. PEIRCE, C. B., and CURTZWILER, F. C. Tuberculous tracheobronchitis; roentgen pathology. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *43*, 153–167.
20. RAABE, R. Der ableitende Bronchus ("bronche de drainage") im Röntgenbild. *Med. klin.*, 1927, *23*, 1448–1450.
21. SHIPMAN, S. J. Bronchial factor in cavitation. *Am. Rev. Tuberc.*, 1938, *37*, 336–345.
22. STEELE, J. D., JR., TRENIS, J. W., and LABOE, E. W. Unexpected cavity closure following reexpansion of lung after ineffectual pneumothorax. *J. Thoracic Surg.*, 1938, *7*, 498–505.
23. VAN ALLEN, C. M., and LINDSKOG, G. E. Obstructive pulmonary atelectasis; problems of pathogenesis and clinical management. *Arch. Surg.*, 1930, *21*, 1195–1213.
24. WARREN, W., HAMMOND, A. E., and TUTTLE, W. M. Diagnosis and treatment of tuberculous tracheobronchitis. *Am. Rev. Tuberc.*, 1938, *37*, 315–335.
25. WESTERMARK, N. On bronchostenosis; roentgenological study. *Acta radiol.*, 1938, *19*, 313–335.
26. WOLF, J. E. Der ableitungsbronchus tuberkulöser Kavernen im Röntgenbild. *Beitr. z. Klin. d. Tuberk.*, 1927, *66*, 700–709.

Vol. 46, No. 3

HERNIA OF THE LUNG

A BRIEF REVIEW AND REPORT OF A CASE

By ADOLPH HARTUNG, M.D., *and* J. W. GROSSMAN, M.D.
Department of Radiology, University of Illinois College of Medicine
CHICAGO, ILLINOIS

HERNIA of the lung is relatively uncommon, only about 200 cases having been recorded as such in the literature to date. Morel-Lavallee[1] in 1845 was the first to make a thorough study of this condition. He reported in detail a series of 32 cases in 1849 and offered a classification which is still accepted in large part. More recently Montgomery and Lutz,[2] Olin,[3] Goodman[4] and Korol[5] have added contributions to the subject.

Hernia of the lung may be defined as a protrusion of the lung and its pleural coverings beyond its usual boundaries. The terms "pneumatocele" and "pneumonocele" have been used synonymously for it but since they merely signify air sacs they are not accurately descriptive of the condition and ought to be discarded. Prolapse of the lung through a ruptured parietal pleura differs from it by lacking a hernial sac. Some of the cases reported probably belong in the latter group according to the descriptions given.

Morel-Lavallee classified pulmonary hernias into congenital and acquired types according to etiology. The former occur primarily because of anomalies of development with defects of the bony or soft tissue structures of the chest wall. They may be apparent at birth but may not make their appearance until later when the lung has expanded completely.

Acquired types of pulmonary hernia are more common than the congenital. They may be traumatic, spontaneous, or pathological in origin. The traumatic is the most frequent type of lung hernia. It may manifest itself immediately after the trauma or at some later time during the course of repair of the traumatized site. Prolonged steady pressure of the expanding lung or sudden increased pressure as from violent exertion may cause the weakened part to give way and permit herniation.

Spontaneous hernia results from lowered resistance in the thoracic wall which is due to developmental factors plus an abnormal or prolonged increase in the air pressure of the lung. It occurs most frequently in such areas of anatomical weakness as the superior aperture of the thoracic cage and in the intercostal spaces in the anterior chest wall medial to the costochrondral junction of the ribs. Such hernias are seen in patients with chronic cough, chronic severe pulmonary emphysema or in individuals subjected to short but severe periods of exertion associated with extreme changes in intrathoracic pressure. The lifting of heavy weights or playing of wind musical instruments may produce it.

In acquired hernias of pathological origin the thoracic wall has been weakened by some destructive process such as abscess of the chest wall, rib caries or malignant disease. Late appearing hernias following trauma might properly be included in this group because of the probable pathologic changes incident to the healing process.

The classification of hernias according to location into (1) diaphragmatic, (2) thoracic or intercostal and (3) cervical groups suggested by Morel-Lavallee has been subjected to criticism. Korol has pointed out that herniation of the lung through the diaphragm is extremely unlikely because of the pressure relationships involved. If there is a congenital or acquired defect of the diaphragm, herniation can occur only from the abdomen into the chest and not in the reverse direction. The same author has also called attention to the fact that mediastinal herniation is properly a pulmonary hernia and ought to be so classified. In view of the

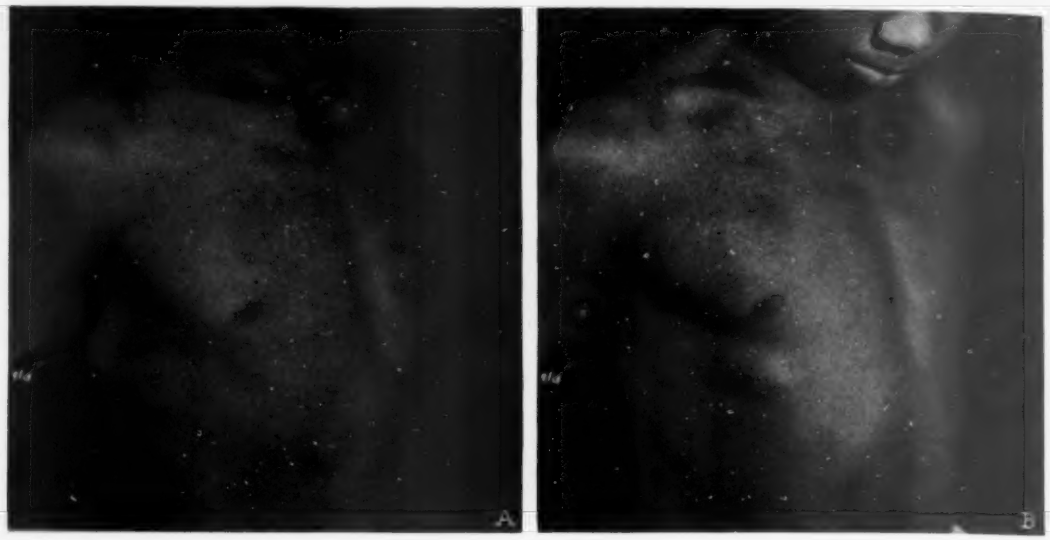


FIG. 1. *A*, photograph of patient at end of moderately deep inspiration. There is no gross abnormality apparent. *B*, photograph made during the performance of the Valsalva procedure. The bulge of the hernia is seen beneath the right nipple.

increasingly frequent occurrence of this condition in connection with modern chest therapy the addition of it will make hernia of the lung far from uncommon.

The cervical type of hernia is rather uncommon. These hernias occur between the scalenus anticus and the sternomastoid muscles, an anatomical weak area where the

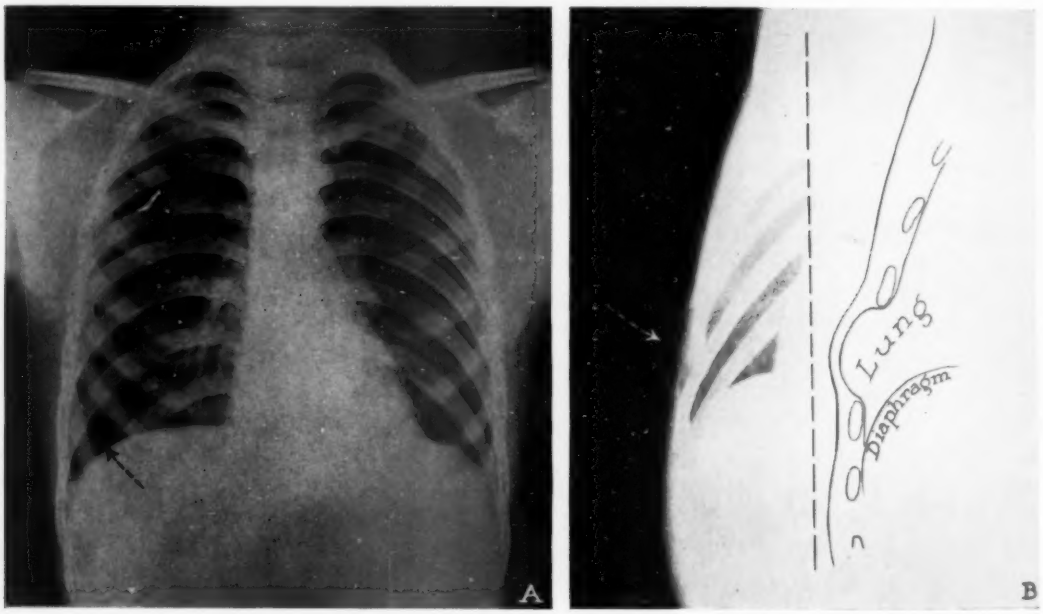


FIG. 2. Roentgenograms of chest made during performance of the Valsalva act. *A*, film made in posteroanterior direction, showing localized radiolucent area above right diaphragm near lateral chest wall in the 6th intercostal space (arrow). This represents the hernia. *B*, roentgenogram made in oblique direction shows the hernia (arrow) projecting beyond the normal boundary of the lung. A sketch is added to illustrate this. The ribs are shown in cross section in the sketch.

lung is least protected by bone and muscle. The protrusion usually presents itself in front of the neck at one side of the larynx.

The great majority of pulmonary hernias, excluding the mediastinal ones, belong to the thoracic or intercostal group. They occur near the sternum internal to the costochondral junction, where the intercostal musculature is thinnest (the external intercostal muscles being absent there entirely), or near the vertebrae at a weak point internal to the rib angle where the internal intercostal muscle ends. The former location is by far the more frequent because the heavier spinal muscles give more protection posteriorly than do the pectoral muscles anteriorly. The case to be reported belongs to the acquired traumatic intercostal type.

CASE REPORT

J. F., male, colored, aged ten, was perfectly well until eighteen months prior to the time he presented himself for examination. At that time, while at play he fell from a bicycle and was struck in the lower right anterior chest. Aside from some local pain and discoloration for a short time after the injury, nothing abnormal was noted and the bruised area healed rapidly. However, about one month later, a bulge was noticed by the patient at the site of injury. The circumstances under which this was first detected are unknown, but it probably was during some act of straining such as coughing or defecation, as judged by the readiness with which the patient demonstrated the bulge simply by forced expiration with the glottis closed.

The important findings on physical examination were: (1) A faintly visible depression in the anterior chest wall in the sixth interspace during quiet respiration. (2) A palpable defect in the interstitial tissues, $1\frac{3}{4}$ inches long with sharply defined margins, extending to either side of the costochondral junction, but more of it being lateral to this point. (3) A bulging, the size of a small hen's egg, protruding from the defect on forced expiration with the glottis closed. The mass was soft, nontender, painless, readily compressible, crepitant, and disappeared promptly on relaxation. It was not visible on quiet respiration (Fig. 1). (4) The skin was freely movable over the hernia and showed no unusual findings.

Roentgen examination during quiet respiration revealed no abnormality. However, during the performance of the Valsalva act, a localized area of radiolucency was visible just above the right diaphragm in the 6th intercostal space anteriorly near the lateral chest wall. In the oblique position the projection of this portion of the lung beyond the remainder of the chest wall could easily be seen (Fig. 2).

REFERENCES

1. Morel-Lavallee. Quoted by Montgomery and Lutz, Olin, and Goodman.
2. Montgomery, J. G., and Lutz, H. Hernia of the lung. *Ann. Surg.*, 1925, *82*, 220–231.
3. Olin, H. A. Hernia of the lung (pneumocele); roentgen study with report of a traumatic case. *Illinois M. J.*, 1932, *62*, 402–410.
4. Goodman, H. I. Hernia of the lung. *J. Thoracic Surg.*, 1933, *2*, 368–379.
5. Korol, E. Hernia of the lung. *Am. Rev. Tuberc.*, 1938, *37*, 39–48.

THE RETENTION OF INTRAVENTRICULAR AIR FOLLOWING ENCEPHALOGRAPHY*

REPORT OF TWO CASES OF UNUSUAL DURATION

By OSCAR A. TURNER, M.D.
ROCHESTER, MINNESOTA
and
BERNARD S. BRODY, M.D.
NEW HAVEN, CONNECTICUT

DESPITE the increasing use of air as a contrast medium, little has appeared in the literature concerning the disappearance of air from the ventricular system. Davidoff and Dyke[1] state that while air shadows are usually still visible in the subarachnoid cisterns twenty-four hours after injection, at the end of forty-eight hours the air has practically all disappeared. Absorption from the ventricles is less rapid. These writers note that after forty-eight hours about two-thirds of the original amount of air has disappeared and that after seventy-two hours, three-fourths is gone. These figures were based upon studies of ventricles with normal (15–20 cc.) capacities. It is generally accepted that, normally, air is practically all absorbed by seventy-two hours. With dilated ventricles, where a correspondingly larger amount of air has been introduced, the absorption is less rapid.

The present report is of 2 unusual instances in which air, introduced through the lumbar subarachnoid space, was visible roentgenographically in the ventricles nine weeks and four weeks after injection.

CASE REPORTS

CASE 1. The patient was a man, aged thirty. He was admitted for the first time in March, 1936, with the complaint of convulsions. He gave a history of having sustained a severe craniocerebral trauma in 1930. At this time he was unconscious for two weeks and recovered after six weeks of hospitalization. He had his first convulsive seizure in 1932, and this was followed by others of increasing severity and frequency despite sedative medication.

Examination at the time of admission disclosed complete anosmia, diminished visual acuity in the right eye, a left homonymous lower quadrant field defect and moderate psychomotor slowing. Encephalography disclosed general dilatation of the ventricular system with slight displacement to the right and a porencephalic defect in the right temporal lobe. At operation there was no definite meningocortical scar but an extremely atrophic temporal cortex and diffuse arachnoid adhesions. The ventricle was uncapped by removing a section of cortex measuring about 5 cm. in diameter. Microscopically, the tissue showed complete destruction of the normal cortical architecture and marked glial replacement.

The patient was admitted for the second time in April, 1939. He had been free from convulsions for about ten months following operation, at which time they reappeared, occurring about twice weekly. Examination showed moderate psychomotor slowing, complete anosmia and a complete left homonymous hemianopia. Under avertin anesthesia, encephalography was again carried out, replacing 180 cc. of cerebrospinal fluid with 170 cc. of air. There was dilatation of the ventricular system with localized enlargement of the right temporal horn which appeared to extend to the edge of a very thin cortex in this region (Fig. 1).

Following encephalography, the patient remained quite drowsy, uncommunicative and had a marked bradycardia. Repeated lumbar punctures were required to control the intracranial hypertension. During the latter part of the hospital stay the patient appeared moderately depressed, restless and was difficult to control.

He entered the hospital for the third time about four days following the previous discharge. He had been taking dilantin and the day before admission began to vomit repeatedly. There had been one convulsion, increasing

* From the Department of Surgery, Division of Neurosurgery, Yale University School of Medicine and the New Haven Hospital, New Haven, Conn.

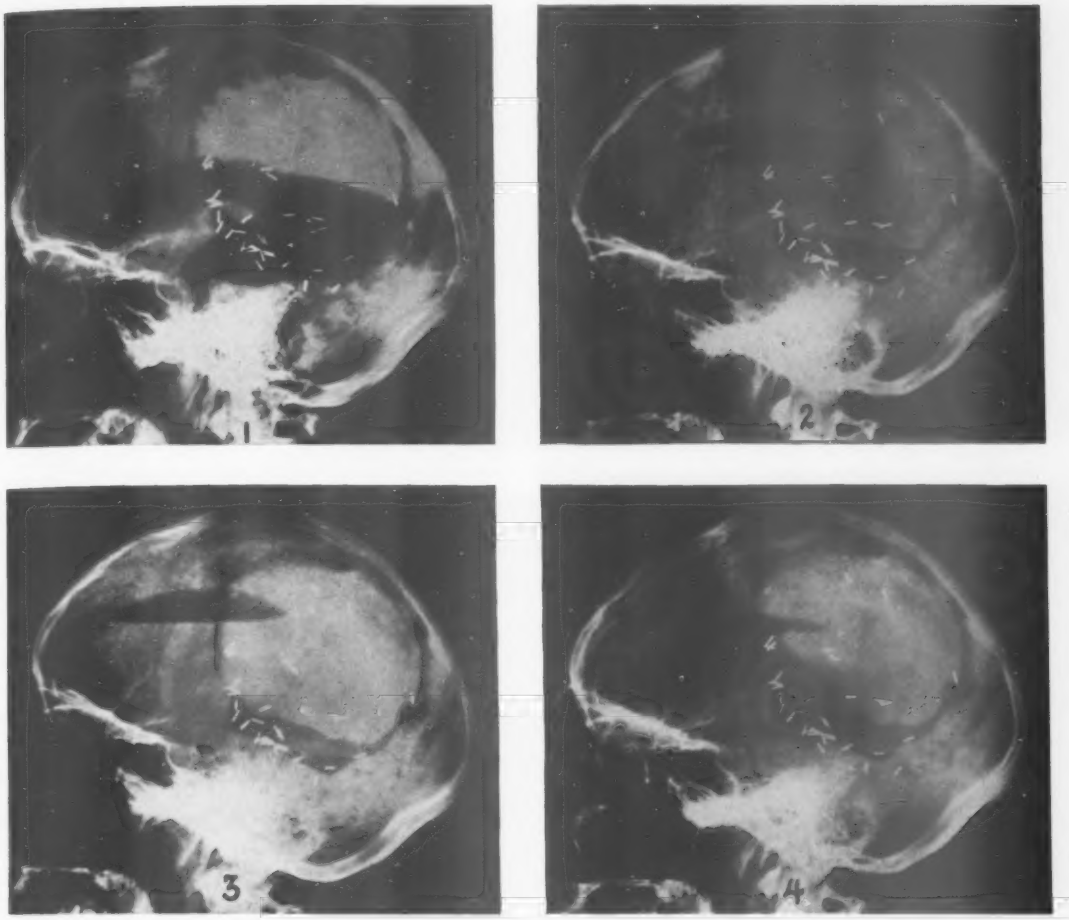


Fig. 1. Case 1. Lateral encephalogram. Note the generalized ventricular dilatation and the localized enlargement of the temporal horn. Fig. 2. Case 1. Film taken four weeks after encephalography. Note the air in both lateral ventricles. Fig. 3. Case 1. Film taken eight weeks after encephalography. Note the relatively small decrease in the size of the air shadow as compared to that in Figure 2. Fig. 4. Case 1. Film taken nine weeks after encephalography and following the initiation of oxygen inhalations. Note the decided decrease in the size of the air shadow.

drowsiness and marked bradycardia. Examination disclosed the patient to be lethargic, stuporous and generally non-responsive. At the time of admission the temperature was 99.2° F., pulse 44, respirations 18 and blood pressure 136/96. There was some stiffness of the neck, generalized hyper-reflexia, haziness of the disc margins and some weakness of the left upper extremity. Lumbar puncture revealed an initial pressure of 300 mm. of water. There was only very slow improvement with repeated spinal punctures until inhalations of 90 per cent oxygen and 10 per cent carbon dioxide were given. Following this, improvement was quite rapid, coincident with the disappearance of air from the ventricular system.

Roentgenographic Findings. Roentgen examination four weeks after encephalography disclosed the presence of residual air in both lateral ventricles (Fig. 2). At this time the patient was lethargic, uncommunicative and quite difficult to handle. Repeat examination eight weeks after encephalography revealed residual air to be still present (Fig. 3). Following this examination oxygen inhalations were instituted. Subsequent examination nine weeks following the injection of air showed that there was yet a small amount present (Fig. 4), but the quantity had diminished considerably as compared to the previous examination. Examination two weeks later gave no evidence of intraventricular air.

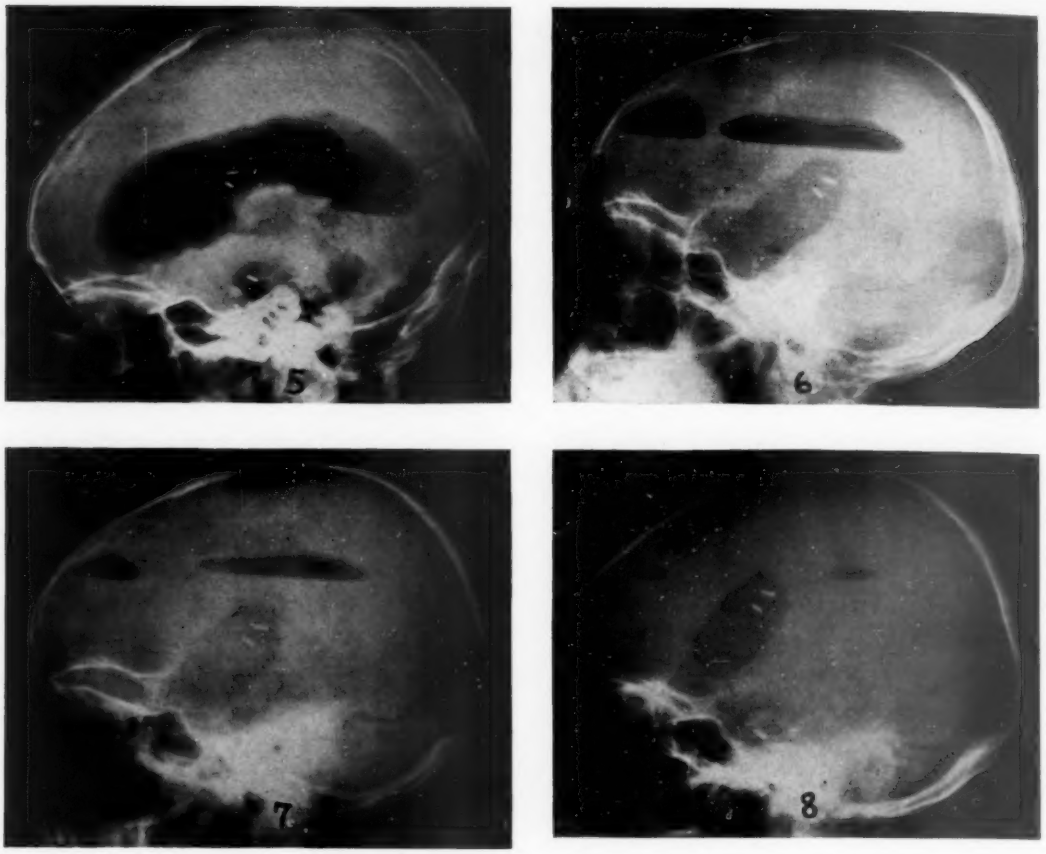


FIG. 5. Case II. Lateral encephalogram. Note the absence of subarachnoid markings and the widely dilated ventricular system. FIG. 6. Case II. Film taken twelve days after encephalography. Note the relatively large size of the air shadow. FIG. 7. Case II. Film taken twenty days after encephalography. FIG. 8. Case II. Film taken almost one month after encephalography and about eight days after oxygen inhalations were started. Note the marked decrease in the size of the shadow as compared to Figure 7.

Comment. The case presents several points of interest. The severity of the symptoms associated with the presence of air within the ventricles was striking as was the alleviation of these same symptoms coincident with the absorption of the air. The beneficial effect of the oxygen inhalations was evident from the relatively rapid disappearance of the intraventricular air following their initiation. The films taken five days after the use of the oxygen (Fig. 4) gave evidence of relatively more absorption than had occurred during the previous four weeks. Another point to be noted is the severity of the symptoms in relation to the small amount of air that was retained.

CASE II. The patient, a colored man, aged thirty-five, was admitted to the hospital in December, 1939, in an unconscious state about one hour after having fallen down a flight of stairs while under the influence of liquor. The ambulance attendant found him unconscious at the scene of the accident; his pulse at this time was 60 and his respirations were 4 to 6 per minute. The pupils were contracted and did not respond to light; the left eye was turned up and to the left. The findings in the accident room were essentially the same except that he began to show signs of responding.

He became progressively more responsive in the next few days. The first spinal puncture done on the third day showed bloody fluid under a pressure of 260 mm. of water; the second done on the fourth day was less bloody and the pressure was 125 mm. of water. The following day a definite third nerve paralysis and

slight weakness of the right side of the body were noted. Within the next twenty-four hours he became progressively more drowsy and ultimately developed a phasic respiratory arrhythmia. On the sixth hospital day he was taken to the operating room where a large subdural clot was evacuated through an enlarged left temporal burr hole.

There was fairly prompt return to consciousness but his speech had not returned to normal one month after operation and in general he seemed considerably slowed, both mentally and physically. An investigation into his social history indicated that he had always been a difficult problem from the behavior standpoint. He had served several jail terms for stealing, was rather over-indulgent in the use of alcohol and had been charged with several illegitimate children.

On February 7, 1940, encephalography was done, replacing 190 cc. of cerebrospinal fluid with 150 cc. of air. The ventricles were all markedly dilated, but the cortical atrophy was particularly marked in the frontal regions where only a thin shell of cortex appeared to remain. There was no definite visualization of the chiasmatic cistern and no subarachnoid air was seen over the cortex (Fig. 5). Roentgenograms taken twenty-four hours after the air injection showed almost complete retention of air in the ventricular system. The reaction to the encephalogram was rather severe and the patient seemed drowsy, complained of headache and had a considerable temperature elevation. This condition continued much beyond the usual time and was relieved only by the initiation of inhalations of oxygen.

Roentgenographic Examination. As has been noted, encephalography on February 7 disclosed general dilatation of the ventricular system with almost complete absence of subarachnoid markings. The fourth ventricle, aqueduct and third ventricle were sharply outlined (Fig. 5). Examination on February 19, twelve days after the introduction of the air, disclosed considerable retention in both lateral ventricles (Fig. 6). Repeat films, on February 27, twenty days after the introduction of the air showed a moderate amount to be still present (Fig. 7). Following this examination inhalations of oxygen were started and films taken March 5, almost one month after encephalography, showed only a very small amount of air in the left lateral ventricle (Fig. 8). Examination eight days later showed no air in the ventricles.

Comment. Here again the severity of the symptoms associated with retention of air in the ventricles is striking, as was the relief afforded by absorption of the air brought about by inhalations of oxygen. The relatively rapid absorption of the retained air following the administration of oxygen can be seen by comparing the various films (Figs. 5–8). It seems likely that the prolonged retention of air in the ventricles in this instance is related to the absence of subarachnoid markings over the cortex.

DISCUSSION

There have been few instances of prolonged retention of intraventricular air described in the literature, although it is probable that this occurs more frequently than would be indicated from the above. Davidoff and Dyke[1] mention a case with markedly dilated ventricles in which air was still seen seventeen days after injection. Foerster[2] reported a case in which the presence of intraventricular air could be recognized three weeks after injection by the succussion sound. This was in a case of internal hydrocephalus in a mentally retarded and epileptic boy, aged twelve, in whom the capacity of the ventricles was judged to be about 1,000 cc. (Case 5). He also mentions the case of a man, aged fifty-six, with a cerebral tumor in which a second roentgenographic examination ten days after the injection of air gave a better encephalographic picture than that obtained immediately after injection (Case 29). As far as we are aware, the first case reported here is the longest in which air has been retained in the ventricles after injection.

The effects of retained air can best be described by referring to the work of Fine and his associates.[3] These authors state: "When atmospheric air accumulates in excessive quantities in body cavities or tissue spaces, it may become a noxious foreign body causing symptoms varying from a mild discomfort to alarming distress." These writers have shown that inhalations of pure oxygen will remove accumulated nitrogen from the body cavities or tissues

in a comparatively short time. An excellent summary of the use of high concentrations of oxygen as a therapeutic measure has been given by Boothby[4] and by Lovelace.[5]

REFERENCES

1. DAVIDOFF, L. M., and DYKE, C. G. The Normal Encephalogram. Lea & Febiger, Philadelphia, 1937.
2. FOERSTER, O. Encephalographische Erfahrungen. *Ztschr. f. d. ges. Neurol. u. Psychiat.*, 1924–1925, *94*, 512.
3. FINE, J., HERMANSON, L., and FREHLING, S. Further clinical experiences with ninety-five per cent oxygen for the absorption of air from the body tissues. *Ann. Surg.*, 1938, *107*, 1–13.
4. BOOTHBY, W. M. Oxygen administration; value of high concentration of oxygen for therapy. *Proc. Staff Meet., Mayo Clin.*, 1938, *13*, 641–646.
5. LOVELACE, W. R., JR. Oxygen for therapy and aviation; an apparatus for the administration of oxygen or oxygen and helium by inhalation. *Proc. Staff Meet., Mayo Clin.*, 1938, *13*, 646–654.

Vol. 46, No. 3

THE ROENTGENOLOGIC DEMONSTRATION OF TUMORS OF THE GALLBLADDER

By J. D. COATE, M.D.
Peralta Hospital
OAKLAND, CALIFORNIA

IT IS interesting to note that there have been very few authors who have reported cases of gallbladder tumors. Kirklin[2] made the original presentation, which was followed by Hefke's[1] case of papilloma and by Kirklin's[3] large series. Moore[4] published 3 cases, one of which was diagnosed as an adenoma and proved surgically. Kirklin's keen interest in cholecystography has stimulated me to be on a constant lookout for these pathologic conditions.

Very little can be added to the information given in the above contributors' reports. Yet, as Kirklin has pointed out, these tumors are not rare and may occasionally be seen if cholecystograms of the finest quality are obtained. It is very important to obtain gallbladder shadows with extremely sharp detail, devoid of any slight motion on the part of the patient. Gas shadows overlying the gallbladder region must be entirely eliminated. The technique must be meticulous, not only in an endeavor to demonstrate these small tumors, but because small, and even large calculi may be overlooked unless great care is used.

The exposure time should be less than one second—preferably not more than one-half second. The instructions to the patient as to the procedure in taking the medication, and also at the time the roentgenograms are made, are very important. Recently, a single 5-gram dose of contrast medium has been used with no increase in the patient's reactions as compared with those following the smaller doses. This drug is given orally the night before and the first set of exposures is made at the fourteen-hour interval. The films are immediately examined to ascertain whether or not their quality may be improved technically, and whether gas obscures the gallbladder region. The recent use of pitressin has been a valuable adjunct, and if gas in the bowel interferes with obtaining a clear shadow, 1 cc. of this drug is given intramuscularly at least one hour before the sixteen-hour exposures are made. As a rule, the patient will have a desire to evacuate the colon in from ten to twenty minutes following the injection, and it is remarkable to note the improvement in the gallbladder shadows with the absence of gas on the remaining films. Since following this procedure very few cases have had to be re-examined because of gas. Of course, there are times when the use of pitressin is contraindicated; such as, in cases of hypertension; marked arteriosclerosis; or when there is a serious cardiac lesion.

Papillomata are often multiple and may occur in any portion of the gallbladder, but they are not usually found in the fundic pole. Adenomata, on the other hand, are almost invariably present in the extreme tip of the fundus and are usually single. Adenomata are also often associated with stones. In this small series of cases, however, no stones were found. The papillomata may be seen in all of the serial examinations, but usually they become more clearly defined when the gallbladder contracts. The adenomata are rarely discovered when the gallbladder is fully distended with the opaque medium; but as the gallbladder contracts following the fat meal the tumor appears as a concave defect with the convexity directed toward the lumen of the gallbladder. These tumors always remain in the same location on successive examinations and, if multiple, they remain in the same relationship to each other. On the other hand, non-opaque stones usually change their positions during the various examinations. This is a differential finding and determines whether the shadow is due

to a stone or a tumor. Hefke also emphasizes the importance of a view tangential to the tumor in order to ascertain whether or not a layer of contrast medium is present between the defect and the wall of the gallbladder.

REPORT OF CASES

CASE I. A woman, aged fifty-three, was nervously upset and developed severe headaches, followed by intractable nausea and vomiting and later by dizziness. Nothing was found to account for these symptoms either organically or functionally. She was hospitalized principally for social isolation. Gastrointestinal examination with a barium meal revealed no evidence of any organic pathology. Cholecystographic examination was made, and this showed a normal appearing gallbladder with excellent concentration of the opaque medium on the fourteen-hour films (Fig. 1). No stones or filling defects were noted on this examination. Following the fatty meal the gallbladder contracted normally, and a definite "slit-like" defect was detected in the fundus on all successive films. The defect became more clearly defined as the gallbladder decreased in size. A tangential position, as suggested by Hefke, may have given a profile view of this tumor on the fourteen-hour films. A definite roentgen diagnosis of adenoma was made. The patient's gastric symptoms, aside from the headache complex, were so few that surgery was not considered at that time. She was discharged from the hospital with a diagnosis of neurosis, arteriosclerosis and adenoma of the gallbladder.

CASE II. A woman, aged forty-three, had a history of recurring, colicky pains in the upper abdomen over a period of three months. In all she had had six attacks and during one she had to be hospitalized and required opiates for relief. Jaundice was never present. Cholecystography by the oral method was done, and this showed a rather small and well concentrated gallbladder shadow at the fourteen-hour examination (Fig. 2). On this examination the fundus was irregular in outline, but no stones or other defects were visible. Following the fat meal the gallbladder contracted to about one-half its original size and a very definite, large, concave defect was present in the tip of the fundus. A roentgenologic diagnosis of adenoma in the fundus was made. Surgery was done by Dr. Sumner Everingham and the gallbladder, which was small and contracted, was removed. There was a diffuse thickening in the entire wall, but more pronounced at the distal end. In the pole of the fundus a large tumor, approximately 8 mm. in

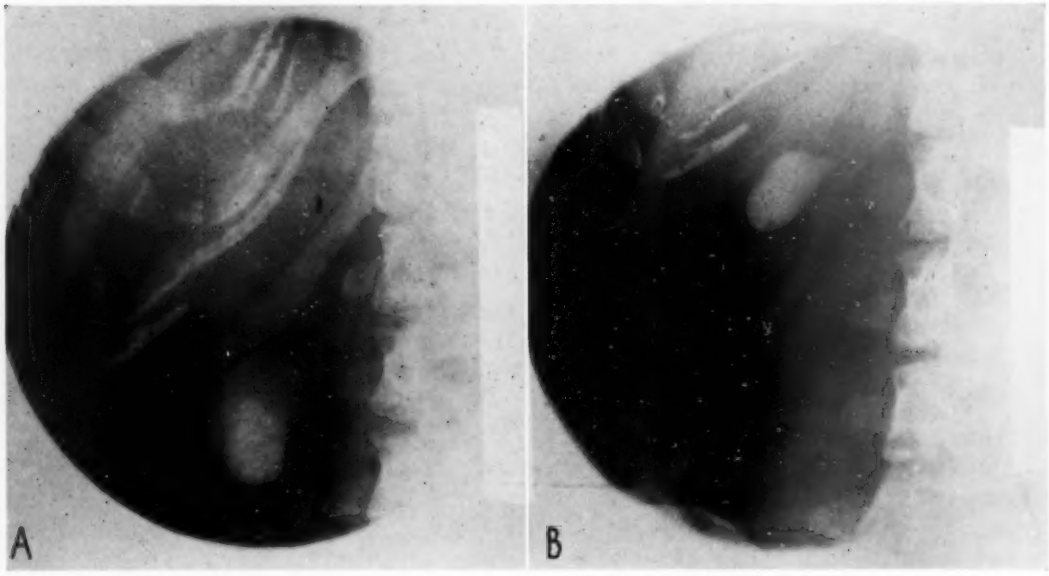


FIG. 1. Case I. *A*, normal appearing gallbladder at fourteen hours; *B*, examination after fat showing the typical adenoma deformity in the fundus.

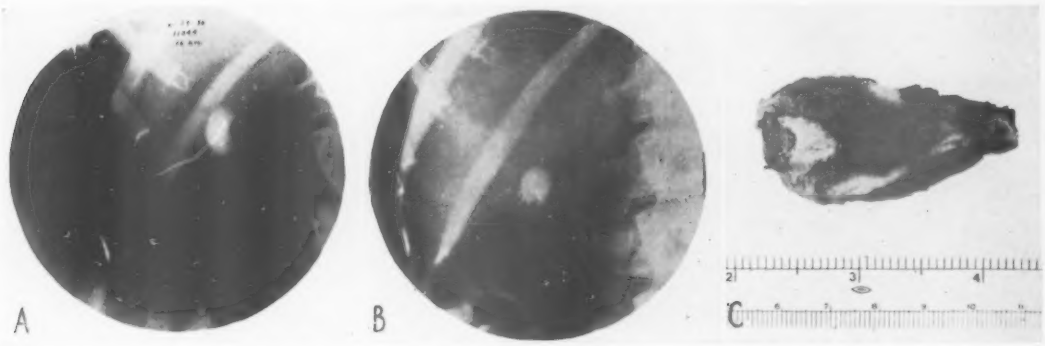


Fig. 2. Case II. *A*, small, well concentrated gallbladder at fourteen hours with slight irregularity of the fundus; *B*, concave defect in tip of fundus suggesting the presence of a tumor; *C*, gross specimen showing the adenoma.

diameter, was found. The vessels throughout were congested and tortuous, and there appeared to be some thrombosis at the tip of the fundus. Pathologic diagnosis of adenoma of the gallbladder, associated with chronic cholecystitis, was made.

Case III. This case was of a woman, aged forty-seven, with indefinite recurring epigastric distress. A pelvic operation was done several years ago. During the past two or three years she has had some gas distress and vague gastric symptoms, but she has never experienced any gallbladder colic. Gastrointestinal examination by means of a barium meal disclosed no evidence of any pathology. Cholecystography revealed a persistent defect on the medial border of the distal end of the fundus (Fig. 3). This defect was present on all the examinations and is more clearly outlined on the films taken after the fat meal. The shadow was very similar to the one seen in Case II, except that it was somewhat smaller. No stones were visible and the gallbladder was of normal density. A roentgen diagnosis of adenoma was made. Upon operation many adhesions of the small bowel to the anterior abdominal wall were found. The gallbladder was removed and its external gross appearance was not markedly abnormal except for some congestion of the vessels noted chiefly about the tip of the fundus. This portion of the fundus appeared to be umbilicated and the gallbladder wall in this area was also greatly thickened. The mucosa was hypertrophied and contained many plaques of cholesterol. In the extreme tip a tumor, measuring approximately

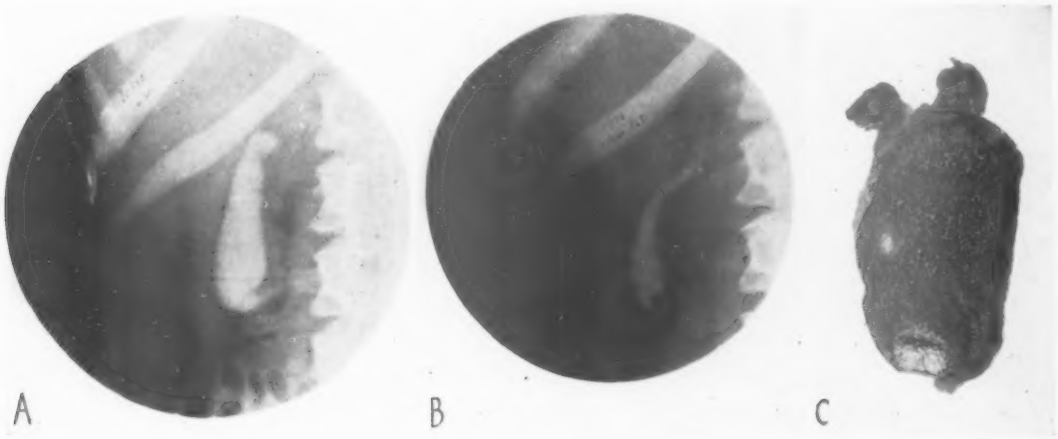


Fig. 3. Case III. *A*, the fourteen-hour examination showing a "slit-like" deformity in the medial wall of the fundus; *B*, at the twentieth hour the defect is more clearly depicted; *C*, gallbladder laid open to show adenoma in situ.

5 mm. in diameter, was found. The pathologic diagnosis was adenoma.

CASE IV. This patient was a woman, aged sixty, who had frequent headaches over a period of years, and intermittent swelling of the lower extremities. She also had increased thirst and had not watched her diet. She had a craving for carbohydrates. During the past two years a general loss of weight had occurred. The patient was hospitalized and complete laboratory and roentgenologic studies were made. A definite diabetes mellitus was found, which was of paramount importance. Gastrointestinal examination by means of a barium meal revealed no evidence of an organic lesion. Cholecystography was done in the usual manner, and showed a well defined, transradiant shadow in the upper portion of the fundus (Fig. 4). This defect had the appearance of a cholesterin stone shadow. Examinations after the fat meal showed this shadow to be in the same position as noted on the previous examination. No other pathologic shadows were observed on any of the examinations. A diagnosis of papilloma was made. Because of the presence of diabetes, and, since there were no clinical findings referable to gallbladder disease, surgery was not indicated. The roentgen diagnosis of papilloma of the gallbladder may never be proved surgically, but it will be of interest to re-examine this gallbladder at a later date in order to confirm these findings. The patient was discharged from the hospital with the diabetes well controlled.

CASE V. This patient was a woman, aged seventy-three, with pain and distress in the upper abdomen. This condition had existed for many years and had become progressively worse. A clinical diagnosis of cholecystitis was made and the patient was advised to enter the hospital for a cholecystographic examination. This examination revealed a fair concentration of the opaque medium on the fourteen- and sixteen-hour films. A well defined, transradiant shadow, simulating a cholesterin stone, was noted in the fundus on all of the films, and became more clearly defined on the examination after the fat meal (Fig. 5). Since the shadow did not change its position on any of the examinations an interpretation of papilloma was given. On operation numerous adhesions were found binding the lower portion of the gallbladder to the duodenum. The gallbladder wall seemed thickened, and did not empty easily. There were three small masses, approximately 2 mm. in diameter, adherent to the mucosa in the fundus. These masses were about the size and shape of a grain of rice, pale in color and moder-

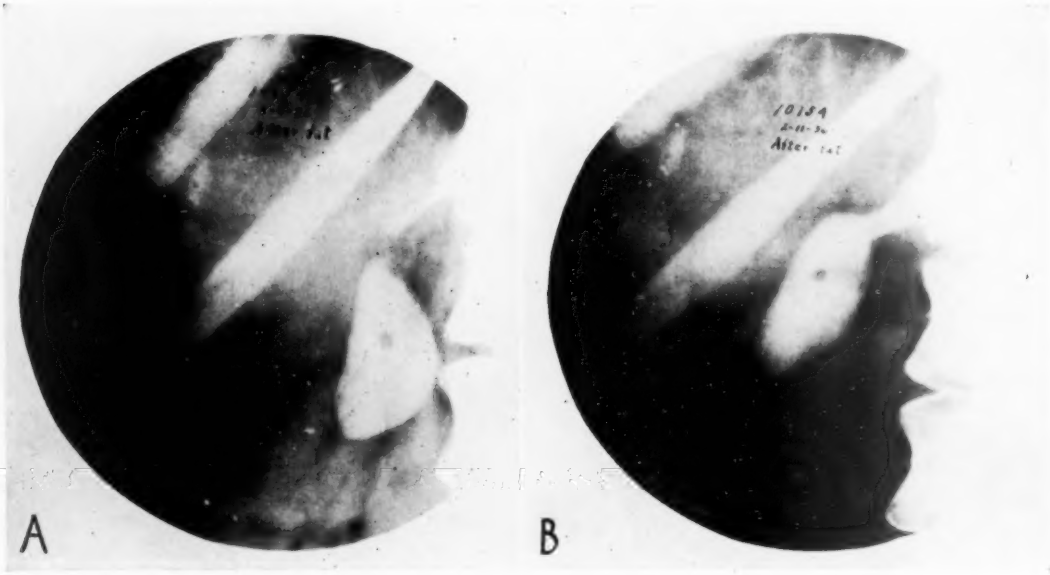


FIG. 4. Case IV. *A*, rounded shadow defect which remained in the same position on all examinations; *B*, examination three days later with the same shadow remaining in the identical position.

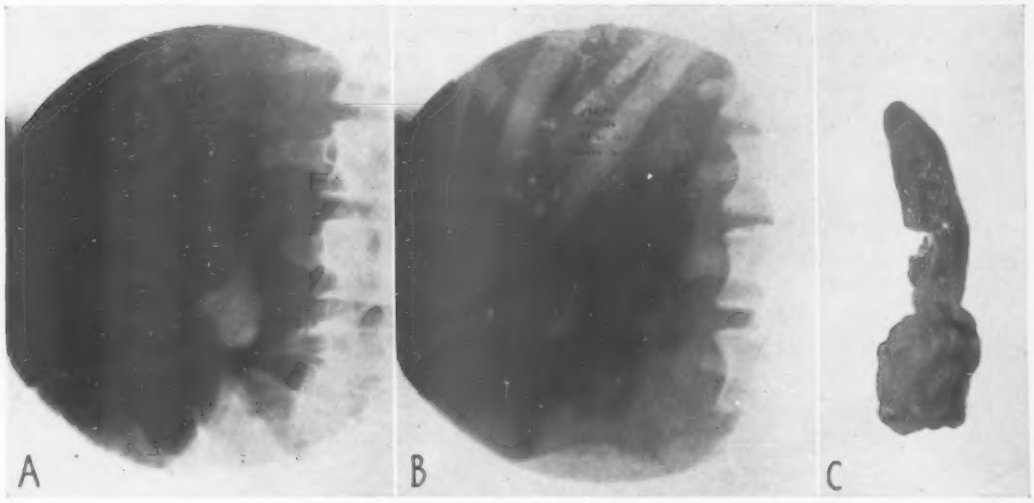


Fig. 5. Case v. *A*, indistinct transradiant shadow in fundus, simulating a cholesterin stone; *B*, the twenty-hour examination shows the same shadow which did not change in position on any of the examinations; *C*, surgical specimen showing the papilloma in the fundic tip, and a second papilloma in the upper portion of the gallbladder. The third tumor was removed for microscopic study.

ately soft in consistency. Otherwise, there was a typical strawberry appearance of the mucous membrane of the gallbladder, and the mucosa showed a moderate amount of thickening. A pathologic diagnosis of multiple papillomata, associated with chronic cholecystitis, was made.

Case vi. This woman, aged thirty-eight, had intermittent attacks of epigastric distress. Some attacks were so severe that she was forced to go to bed. The pain radiated to the right shoulder and to the epigastric region. She also complained of gas and could not tolerate fats. The patient lost 15 pounds in weight. She was hospitalized elsewhere. Cholecystography was done and described as "poorly functioning, with possible stones." She was opposed to operation and was placed on a gallbladder medical regimen. The patient showed no improvement with medical treatment, her icteric index increased to 19

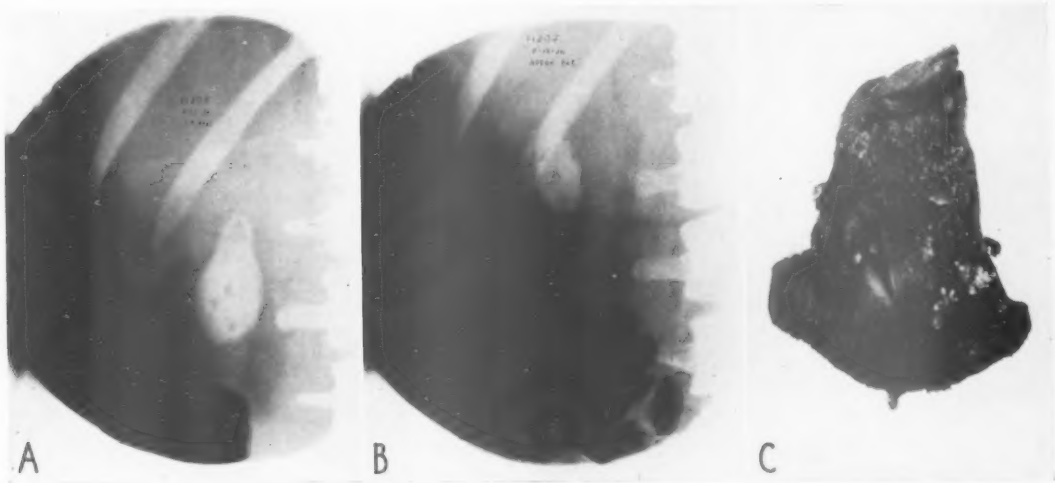


Fig. 6. Case vi. Multiple shadow defects representing papillomata. Although they are visible at the fourteenth and sixteenth hours *A*, they are more clearly depicted at the twentieth hour and many more become visible in the upper portion of the gallbladder *B*; *C*, gross specimen showing papillomata in situ.

mg., and a re-examination of the gallbladder was advised. The usual procedure was followed in this examination and an excellent shadow of the gallbladder was revealed on the fourteen- and sixteen-hour films. There were three distinct transradiant shadows visible in the fundus (Fig. 6). Examinations after the fat meal revealed not only these same shadows but several other similar ones scattered throughout the gallbladder. It was interesting to note that all these shadows remained in the same relative position to each other and in the same respective positions in the gallbladder. A definite roentgen diagnosis of papillomatosis of the gallbladder was given. A cholecystectomy was performed and a few adhesions were noted around the cystic duct. No stones were palpable, and occasional nodulations were observed within the wall. Grossly, the specimen showed many adhesions on the serosal surface and the wall was thickened and fibrous. The mucosa was hypertrophied and contained many incrustations of cholesterol. In the fundus approximately eight papilliferous masses, ranging from 2 to 3 mm. in diameter, were noted apparently attached to the mucosa. These masses were pale, soft, spongy and of a finely granular structure. They also appeared to be in the nature of cholesterol deposits. A pathologic diagnosis of multiple papillomata associated with low grade chronic cholecystitis, was made.

CASE VII. Female, aged forty-two, complained of gastric distress with pain in the upper right quadrant which was extremely marked following heavy meals. Abdominal palpation revealed marked muscle spasm in the right upper quadrant. Cholecystography revealed a well concentrated gallbladder with two small transradiant shadows in the fundus and a larger shadow in the neck of the gallbladder. A roentgenologic diagnosis of "normally functioning gallbladder with multiple minute papillomata" was given. Cholecystectomy and appendectomy were done. A long, fibrous, and densely adherent appendix was found extending down into the pelvis. There were extensive fibrous adhesions binding the transverse colon to the surface of the gallbladder. No stones were palpable. The pathologic examination of the gallbladder showed a papilloma in the proximal portion of the gallbladder measuring 9 mm. in diameter, and two smaller ones in the fundus, measuring 3 mm. in diameter. There were no stones present.

CASE VIII. Female, aged thirty-nine, complained of indigestion from time to time with considerable gas. These symptoms continued and became progressively worse with intermittent attacks of icterus. One month prior to the examination she began to have pain below the right shoulder blade which radiated down the right arm. Cholecystography revealed excellent concentration of the opaque medium at the fourteen- and sixteen-hour examinations. The gallbladder was normal in size and shape and there were no shadows to indicate the presence of biliary calculi on the immediate roentgenograms. Following the fatty meal the gallbladder contracted normally and a small, rounded, transradiant shadow appeared in the tip of the fundus, becoming more prominent as the gallbladder continued to contract. A roentgenologic diagnosis of a "normally functioning gallbladder with a small adenoma in the fundal tip" was made. At surgery the gallbladder was found to be large, pale in color, thickened, and the cystic duct was definitely bound to the duodenum with rather dense adhesions. The pathologic report showed a markedly trabeculated mucosa with the wall thickened, fibrous and edematous. There were no stones present. A raised and somewhat umbilicated mass, 1 cm. in diameter, was visible in the tip of the fundus. The microscopic section through the mass in the fundal tip showed an adenomatous pattern with cells of high columnar type. They were well differentiated and were held in a fibrous stroma. There was no microscopic evidence of malignant degeneration. Pathologic diagnosis was "benign adenoma of the gallbladder, and chronic cholecystitis."

Grossly, all the tumors here reported appear as small, thickened nodules, measuring from 2 mm. to 1 cm. in diameter, and are located on the mucosal surface of the gallbladder. The papillomata are usually attached to the gallbladder wall by a fine, filamentous pedicle, which may be brushed off and the tumor itself mistaken for a small deposit of cholesterin material.

Interesting microscopic studies of these tumors were made by Dr. Paul Michael, who reports the following pathologic findings:

The adenomata show a fairly normal, intact and moderately flattened mucosa throughout the gallbladder (Fig. 7). In the region of the

raised mass there is a heaping up of numerous glands lined by high columnar epithelium. In the upper surface of this mass the glands conform to the papilliferous pattern and are arranged on a somewhat branching stroma. The stroma is delicate and contains a few round cells and numerous engorged vascular channels. These glands also extend into the wall down into the muscle layer. In this zone there are numer-

Fig. 7. Photomicrograph of the adenoma. The glandular structure can be seen deep in the muscularis.

ous round cells, macrophages and markedly engorged blood vessels. These cells extend out to the serosa. The basement membrane of all the glandular elements appears preserved throughout. There are no mitotic figures seen. The mass appears fairly discrete but is not encapsulated.

The microscopic sections taken through the papillomata show a very narrow, delicate stalk lined by a high columnar epithelium. The papillomatous mass at the end of the stalk is also lined by a high columnar epithelium resting upon an intact basement membrane. The stroma consists essentially of large, clear, lipoid cells with small nuclei having a xanthomatous appearance (Fig. 8). Scattered through the stroma are occasional cholesterol crystals.

Clinically, these tumors are silent, and the symptoms are usually referable to the

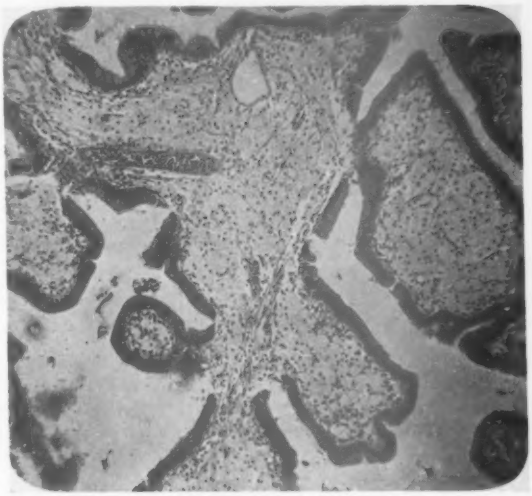


Fig. 8. Photomicrograph of microscopic section of the papilloma.

accompanying cholecystic disease; and, as Wellbrock[5] has reported, the incidence of malignant lesions is very low.

Malignant degeneration has never been found in any of the tumors which have been reported. Primary cancer of the gallbladder, however, is not infrequent and all adenomata may be considered potentially malignant. Above all, we wish to stress the importance of distinguishing these tumors from transradiant stones.

REFERENCES

1. Hefke, H. W. Die diagnose von Papillomen der Gallenblase mittels Cholezystographie. *Röntgenpraxis*, 1931, *3*, 871–873.
2. Kirklin, B. R. Cholecystographic diagnosis of papillomas of the gallbladder. Am. J. Roentgenol. & Rad. Therapy, 1931, *25*, 46–50.
3. Kirklin, B. R. Cholecystographic diagnosis of neoplasms of the gallbladder. Am. J. Roentgenol. & Rad. Therapy, 1933, *29*, 8–16.
4. Moore, C. Cholecystographic diagnosis of papillomas and tumors of the gallbladder. Am. J. Roentgenol. & Rad Therapy, 1935, *33*, 630–635.
5. Wellbrock, W. L. A. Occurrence and possible significance of adenoma of the gallbladder. *Am. J. Surg.*, 1934, *23*, 358–360.

DYSOSTOSIS MULTIPLEX

By MAXIMILIAN J. HUBENY, M.D., F.A.C.R., F.A.C.P., *and*
PERCY J. DELANO, B.S., M.D.
From the Department of Roentgenology, Cook County Hospital
CHICAGO, ILLINOIS

IN 1919, Gertrud Hurler,[14] writing from the Universitätskinderklinik at Munich, described 2 cases which appeared to constitute a new clinical entity. Their common characteristics included a large, asymmetric skull; a broad, grotesque face; corneal opacities; enlargement of the liver and spleen; mental deficiency; delayed epiphyseal ossification, and a kyphos exhibiting unusual features in the lateral roentgenogram.

Hurler considered, in her original monograph, that these 2 cases constituted another in the group of osseous and cartilaginous dystrophies, making a fourth with the three then clinically and roentgenologically recognized, i.e., dystrophia periostalis hyperplastica, dysostosis craniofacialis, and dysostosis cleidocranialis.

For a time Hurler's publication seems to have attracted little attention, and for ten years thereafter the literature is almost barren of any contributions on the subject. In 1928 Brailsford[3] presented, before the Royal Society of Medicine, roentgenograms of a child which exhibited very unusual osseous changes, "the like of which he had not seen before—the case described by Silverskiöld in 1926 as a 'forme fruste' type of chondrodystrophy bearing the nearest resemblance." He published the material the following year, and in the same year Morquio[22] published details of a similar dystrophy.

Brailsford named the condition "chondro-osteo-dystrophy," which term has been largely employed by the English writers since, and Morquio described the findings in his case as a "dystrophy osseuse familiale." Morquio's paper has been widely quoted, and perhaps the majority of contributions on the subject appearing during the last ten years have borne the title "Morquio's disease."

CASE REPORT

On November 1, 1939, there was admitted to the Cook County Hospital C. R., a male colored child, aged seven, whose outstanding finding was a kyphos involving the upper lumbar area. He was sent for routine roentgenologic examination, and the peculiar deformity of the vertebral column, which was not considered readily classifiable in our department, led to the request for additional films.

The findings in the other films were unusual, and the first report which was dictated is quoted verbatim:

> The dorsal and lumbar vertebrae have a peculiar contour. There is an irregularity of the anterior portions of the bodies, and a number of the dorsal vertebrae have a markedly convex superior and in some cases inferior aspect. Two of the vertebral bodies, possibly the first and second lumbar, are particularly deformed, there being a decrease at the intervening intervertebral space with considerable kyphos at this level.
>
> Film of the chest suggests a slight possible widening of the mediastinum in the thymic region but no definite evidence of pulmonary pathology. The rotundity of the posterior portion of the ribs seems to be somewhat less than normal, the inferior costovertebral angles being about 50 degrees.
>
> The pelvis has a peculiar contour, there being an inward displacement of the pelvic bones at the level of the acetabula. There is a consequent marked widening of the joint spaces at the hips with a suggested slight subluxation of the femoral heads. There is also a flattening of each femur with a slight irregularity. A slight separation is present at the symphysis pubis. There appears to be a coxa valga deformity.
>
> There are only two carpal bones, the centers of ossification for the rest having not as yet appeared. There is an irregularity in the proximal ends of the metacarpal bones. The epiphyses are rather small. This is particularly true of the epiphysis of the first metacarpal on each hand. The proximal phalanges and metacarpals are rather broad. This appears to be true of the proximal portion of the second phalanges.
>
> The lower epiphysis of each radius is rather small and no epiphysis has yet appeared in the lower end of each ulna. The proximal epiphysis of each radius is rather small and the proximal half of each radius

is rather broad as compared with the distal portion of the bone. There is no evidence as yet of ossification of the epiphysis of the olecranon process. The capitellum is rather small.

The centers of ossification for the patellae have not as yet appeared. Neither has the center for the proximal epiphysis of either fibula.

It was then decided that the case fitted clearly into the group of chondro-osteodystrophy, or Hurler's syndrome, or Morquio's disease, or, to use the term which has been current since about 1933, "dysostosis multiplex."

The clinical and laboratory findings relative to this patient are appended here:

Mentality, normal.

Eyes: No evidence of corneal opacities. Fundi, normal.

Nose and throat: Normal.

Blood pressure, 128/96. Blood picture: hb, 93 per cent; color index, 1+; leukocytes, 8, 100; red blood cells, 4,150,000; differential: polymorphonuclears, 71 per cent; eosinophils, 2 per cent; lymphocytes, 25 per cent; monocytes, 2 per cent. Kahn reaction, negative.

Fig. 1. Here the characteristic deformity of the vertebrae is well illustrated. The actual defect in ossification is above and below on each vertebral body, leading to the hook-like projection of the central portion anteriorly. Note the kyphos in the upper lumbar area.

Fig. 2. The acetabula are notably deficient. There is consequent widening of the joint spaces at the hips. No actual subluxation is believed present. The femoral heads are flattened and irregular. The gap at the symphysis is wide. Some bilateral coxa valga appears present.

Urinalysis: Specific gravity, 1.020; reaction, acid; albumin and sugar, negative; acetone, negative; no casts; no occult blood.

Blood chemistry: Blood sugar, 41; serum phosphatase, 14.65; phosphorus, 7.57; calcium determination, insufficient blood, patient leaving the ward before determination was repeated. Total protein, 9.81; albumin, 5.52; globulin 2.29.

Basal metabolic rate: Failed for lack of cooperation by patient.

Spinal fluid: Kahn test, negative; spinal sugar, 63; spinal NaCl, 670; total protein, 23.

Before proceeding with a detailed consideration of this disease entity, since it may already have been noted that our case had normal mentality, normal skull, and no corneal opacities, it may be remarked that it conforms more to the Morquio type, in which these findings are absent, than to the original Hurler type, in which it was

FIG. 3. Though the age of the child is seven, only two carpal bones are present. The proximal ends of the metacarpals are irregular. The epiphyses are rather small. This is particularly true of the epiphysis of the first metacarpal on each hand. The metacarpals and proximal phalanges are rather broad, as are the bases of the second phalanges. The lower epiphysis of each radius is small and no epiphysis is present for either ulna. The proximal half of each radius appears broadened. The capitellum is small.

considered that they ought rather uniformly to be present.

Since a great many findings, some of them rather varied in character, have been reported by various observers, it may be best to take up a consideration of this entity under separate headings, in order to correlate more clearly the symptoms and physical findings which are most constantly noted.

ETIOLOGY AND PATHOLOGY

Males and females are affected equally. The parents have in all recorded cases been healthy. No nationality has been predominantly affected.

Because of the enlargement of the liver and spleen frequently reported, the similarity to Niemann-Pick's disease, and to the other lipoid dystrophies, has been suggested.[16] Foam cells have been found in the reticulo-endothelial system, but this finding is not now considered as significant as when first reported.

Autopsy findings have been few. One complete autopsy has been described in detail.[1] This case had chondro-osteal changes described as classical, without, however, having any enlargement of liver or spleen. There was no evidence of lipoid storage in the reticulo-endothelial system, and no foam cells. In the brain, ganglion cells were abnormal, their cytoplasm being distended by an abnormal substance, the Nissl granules reduced in number and crowded to one portion of the cell, and the nucleus dislocated to one side, but little affected.

Tuthill studied the brain in Hurler's first case.[4] He regarded the anatomic findings as compatible with amaurotic family idiocy. Macroscopically there was edema of the brain and internal hydrocephalus with atrophy of the temporal lobes, and tubercles were found in the frontal and parietal lobes. Microscopically the optic nerves were demyelinated, with a heavy mantle of fat granular cells; the brain showed lipoid-containing cells sparsely scattered throughout the white substance, and generalized thinning of the myelin sheaths.

From the above findings, and from some other data, Ellis, Sheldon and Capon[7] reached the conclusion that the disease bears a certain relationship to the lipoid dystrophies.

Hirsch[12] summarized the condition as one in which "disturbances in epiphyseal ossification are associated with a malacia which produces definite deformity in the ends of the bone."

Ruggles[25] reported cases in 1932, in which he pointed out that the disease, which had already been likened to achondroplasia, differed from it in certain essential details: while, in achondroplasia, the epiphyses close early, in dysostosis multiplex they are late in appearance and delayed in closure.

SYMPTOMS AND PHYSICAL FINDINGS

Brailsford[3] has given an excellent picture of the disease. He points out that the lesion which first attracts the parents' attention and causes them to seek medical advice is in most cases a kyphos in the dorsolumbar area. Later, such joints as the knee, ankle and wrist appear to be swollen, as in rickets. When the child has reached the age of three years the neck appears to be markedly shortened and the thorax prominent, a feature which becomes more distinctive with age, for, owing to the profound dystrophic changes at the cervicodorsal junction growth is almost completely checked here while the head and thorax appear to develop at an almost normal rate. By the age of five or six years the patient has developed into a dwarf having very characteristic appearances, the most striking of which is the marked shortness of the trunk compared with normally developed limbs. The head sits closely on a thorax which is prominent anteriorly, and from the short body the lower limbs in particular appear to have developed to an abnormal length. A marked kyphos may now be present in the dorsolumbar area. The limb joints are swollen and present a superficial resemblance to rickets.

Fig. 4. The proximal radial epiphysis is small; the upper end of the ulna appears irregular, and no ossification is noted in the olecranon.

Fig. 5. In our case the skull showed no definite departures from the normal.

As to roentgenographic appearances, Brailsford emphasizes the irregular growth of the epiphyses, though primary and secondary ossific centers are involved in the process. All the primary ossifications may show irregularity of their growing extremities. This is particularly noted in the vertebral bodies where the defective development of the articular processes may lead to displacement with kyphotic deformity. The characteristic deformity is produced by failure of development at the superior and inferior margins of the vertebrae, the central portion appearing for this reason to project with a process which in some cases is hook-like.

During adolescence the epiphyses for the superior and inferior surfaces of the vertebral bodies begin to appear as multiple, ill-defined ossific nuclei in the spaces above and below the projecting tongues of the middle thirds of the anterior surfaces. The superincumbent weight on the poorly developed bone causes pressure deformities.

In the infant all the articular cartilages appear to be markedly thickened, for the

spaces between the bony contours is much increased. The extremities of the diaphyses are irregular and the ossific nuclei for the epiphyses first appear as multiple anomalous islands of bone on the other side of the thickened metaphyses. These nuclei gradually fuse, but in those joints subjected to normal pressure the incapability of the disorganized bone to withstand the normal stresses and strains leads to distortion and compression of the involved bone.

As one would expect, Brailsford concludes, the most conspicuous changes are often to be seen in the hip joints.

The findings relative to the skull have shown wide variation.

Putnam and Pelkan[20] describe acrocephaly, oxycephaly and brachycephaly, but point out that the most typical deformity is scaphocephaly. Prominence of the supraorbital ridge and lateral bossing of the temporal bones have been mentioned. One of Hurler's cases showed an exostosis at the base of the skull. An enlarged sella has been noted. Prominence of the mandible has been described. Hypertelorism has been listed among the findings frequently, and the eyes may be set low in the head. The bridge of the nose is sometimes depressed, and when this condition is present, it is often accompanied by a purulent nasal discharge.

It is notable that these skull changes may be entirely absent, the other findings in the skeleton being characteristic of dysostosis multiplex, and this type is presented in the cases first described by Morquio and Brailsford.

Marked platyspondyly was described in one case.[5] The short trunk, the crouching position, the shelf-like protrusion of the chest, have been emphasized by Meyer and Brenneman.[21] These observers also point out that the head, as well as the mental capacity, may be quite normal. They add to the list of previously described symptoms the finding of a cystic, bulbous lower fibular extremity.

Loose bodies in the hip joints have been recorded.[10]

Hirsch[12] points out that the carpal and metacarpal changes described by Morquio are the same as those described by Brailsford, one of the most outstanding of these being in the first, which may have a double-nucleated distal epiphysis.

Kressler and Aegerter[16] mention the occurrence of ascites and edema of the lower extremities; as well as visual disturbances and progressive loss of the psychic function which may go on to idiocy of the Tay-Sachs type.

Periosteal thickening has been noted.[24] Some observers record limitation of extension in the joints, as well as limitation of flexion.

DIFFERENTIAL DIAGNOSIS

Polyarthritis of infancy when present in a chronic form may occasion difficulty. Repeated roentgenograms must be made, and the characteristic changes at the ends of the bones searched for. Associated symptoms of fever or other evidence of infection may help in identifying polyarthritis, and the periarticular symptoms in arthritis should be much greater than in dysostosis multiplex.

Hypothyroidism may cause confusion, because here the outstanding finding is delay in the appearance of epiphyseal centers, but in hypothyroidism the shafts of the bones may have a thicker, more compact cortex than in dysostosis multiplex, and are also often more slender than normal, gradually expanding to normal width at the extremities, and the spinal deformity of dysostosis multiplex is absent.

Pott's disease is often suggested when the first symptom to attract attention is the kyphos, but the roentgenogram should show clearly defined characteristics of dysostosis multiplex when the condition has progressed to the stage of kyphos formation. Roentgenography of the other bones should show associated changes sufficient to rule out tuberculosis without much difficulty.

Achondroplasia results in a form of dwarfism which externally is not unlike

that of dysostosis multiplex, and the phalanges are short and thick; however, the body appears long in proportion to the length of the legs in achondroplasia, the reverse being true in dysostosis multiplex, and in achondroplasia the epiphyses tend to fuse at a normal time or even earlier.

Ollier's disease, or diaphyseal aclasia, shows deformities at the ends of the bones not unlike those described in some cases of dysostosis multiplex, particularly in one of Brailsford's cases. However, critical inspection will show the enchondromatous character of the former condition, and the spinal changes are absent. Some writers include multiple cartilaginous exostoses under the heading of Ollier's disease, separating the disease into two forms, enchondroplasia and ecchondroplasia, accordingly as it conforms to the type first described by Ollier or to the exostotic type, but in neither are the epiphyseal or vertebral changes characteristic of dysostosis multiplex.

Scheuermann's disease attracts the attention of the clinician to the spine, and the roentgenogram shows a variety of changes, so varied that some of them might be mistaken for the peculiar beak-like deformity of dysostosis multiplex; but here the changes are confined to the spine, and upon studying the films it will be noted that the upper, and in some cases the lower vertebral epiphyses show condensation and perhaps fragmentation resembling that of osteochondritis at other sites, and there is usually an associated widening of the metaphyseal area. The body itself, where it borders on these metaphyses, may appear splayed out by pressure indicating softening of the bone, and an indentation may appear in the mid-area of the upper and lower borders of the vertebral bodies due to herniation of the nucleus pulposus.

Rachitis tarda produces spinal deformities which are a result of the extreme malacia which characterizes some of these cases. There may be pseudofractures and marked disc impressions, but the deficiency above and below noted in the vertebral bodies in dysostosis multiplex will not be found, and the patient in rachitis tarda frequently shows associated changes of chronic glomerulonephritis.

Craniofacial dysostosis may have an oxycephalic cranium, but the maxilla is atrophic and there is usually a parrot-beak type of nose, and exophthalmos. Osseous sutures are obliterated in the roentgenogram, there is a thin skull and sinking in of the middle fossa with a nearly vertical orientation of the skull.

Cleidocranial dysostosis may show failure of ossification of large areas in the skull, failure of fusion of the fontanelles and sutures, the presence of multiple wormian bones, and the deciduous teeth may be retained.

Arachnodactyly often shows an associated deformity of the skull similar to the skull deformity in the Hurler type of dysostosis multiplex, but the appearance of the phalanges is characteristic and should be enough to make the diagnosis.

COURSE AND PROGNOSIS

The condition has not yet been observed over sufficiently long periods to predicate much as to life expectancy; yet, we know that it is compatible with attaining adult age. One factor here which seems of major importance is whether or not the depression of the bridge of the nose is present; for when it is, there is usually a severe and often purulent nasal discharge which remains intractable, and which tends to extend to the sinuses and the upper respiratory tract.

TREATMENT

Orthopedic management of the deformities is all that has been of service to date. Various approaches through endocrine therapy have been without result.

SUMMARY

Dysostosis multiplex is a congenital disease characterized by interference with ossification, and which leads to degenerative changes in cartilage. The active stage of the dystrophy appears to cease as the time for

fusion of the epiphyses and diaphyses approaches, but the pressure deformities remain as evidence that the dystrophy has existed. Prominent among the characteristic lesions are wedge-shaped deformities of the vertebrae, failure of appearance of epiphyseal centers and delay in their ossification, marked shortening of the neck due to cervicodorsal deformity, which also leads to an appearance of a shelf-like protrusion of the upper thorax, and marked shortness of the trunk as compared with the limbs. Deformities of the skull are variable and inconstant; there may be scaphocephaly or oxycephaly and depression of the bridge of the nose, and corneal opacities are found in some cases; when these skull and eye changes are present the deformity corresponds more nearly to the type originally described by Hurler; when they are absent the type falls more into the group described by Brailsford and Morquio.

The literature appears to contain reports of about twenty-seven cases to date.

REFERENCES

1. ASHBY, W. R., STEWART, R. M., and WATKIN, J. H. Chondro-osteo-dystrophy of the Hurler type (gargoylism): pathological study. *Brain*, 1937, *60*, 149–179.
2. BARNETT, E. J. Morquio's disease. *J. Pediat.*, 1933, *2*, 651–656.
3. BRAILSFORD, J. F. The Radiology of Bones and Joints. William Wood & Co., Baltimore, 1935.
4. BROWN, D. O., and MACDONALD, C. Three cases of familial osseous dystrophy. *Australian & New Zealand J. Surg.*, 1933, *3*, 78–88.
5. CRAWFORD, T. A case of Morquio's disease. *Arch. Dis. Childhood*, 1939, *14*, 70–77.
6. DAVIS, D. B. and CURRIER, F. P. Morquio's disease. *J. Am. M. Ass.*, 1934, *102*, 2173–2176.
7. ELLIS, R. W. B., SHELDON, W., and CAPON, N. B. Gargoylism. *Quart. J. Med.*, 1936, *5*, 119–139.
8. ENGEL, D. Dysostosis multiplex: Pfaundler-Hurler syndrome. *Arch. Dis. Childhood*, 1939, *14*, 217–230.
9. FREEMAN, J. Morquio's disease. *Am. J. Dis. Child.*, 1938, *55*, 343–355.
10. GOLDING, F. C. Chondro-osteo dystrophy. *Brit. J. Radiol.*, 1935, *8*, 457–465.
11. HÄSSLER, E. Das Krankheitsbild der Dysostosis enchondralis. *Monatschr. f. Kinderh.*, 1937, *68*, 254–256.
12. HIRSCH, I. S. Generalized osteochondrodystrophy; eccentrochondroplastic form. *J. Bone & Joint Surg.*, 1937, *19*, 297–313.
13. HUBER, J., LIEVRE, J. A., and NERET, MME. Acrocéphalie ou dysostose cranio-faciale fruste chez deux jumeaux. *Bull. et mém. Soc. méd. d. hôp. de Paris*, 1938, *54*, 595–598.
14. HURLER, G. Ueber einen Typ multipler Abartungen, vorwiegand am Skelettsystem. *Ztschr. f. Kinderh.*, 1929, *24*, 220–234.
15. JACOBSEN, A. W. Hereditary osteochondrodystrophia deformans. *J. Am. M. Ass.*, 1939, *113*, 121–124.
16. KRESSLER, R. J., and AEGERTER, E. E. Hurler's syndrome (gargoylism). *J. Pediat.*, 1938, *12*, 579–591.
17. LANGE, F. Ueber atypische Chondrodystrophie (Achondroplasie) und über eine noch nicht beschriebene angeborene Wachstums störung des Knochensystems: metaphysäre Dysostosis. *Ztschr. f. orthop. Chir.*, 1934, *61*, 253–286.
18. LIEBENAM, L. Beitrag zur Dysostosis multiplex. *Ztschr. f. Kinderh.*, 1937, *59*, 91–123.
19. LIEVRE, J. A. La classification des dystrophies osseuses et l'ostéose parathyroïdienne. *Presse méd.*, 1932, *40*, 234–236.
20. MARIANTSCHICK, L. P. Ueber die Knochendystrophie. *Arch. f. klin Chir.*, 1931, *168*, 349–370.
21. MEYER, H. F., and BRENNEMANN, J. A rare osseous dystrophy (Morquio), *Am. J. Dis. Child.*, 1932, *43*, 123–135.
22. MORQUIO. Sur une forme de dystrophie osseuse familiale. *Arch. de méd. d. enf.*, 1929, *32*, 129–140.
23. PUTNAM and PELKAN. Quoted by Ellis, Sheldon and Capon, ref. 7.
24. REILLY, W. A. Dysostosis multiplex. *Endocrinology*, 1938, *22*, 616.
25. RUGGLES, H. E. Dwarfism due to disordered epiphyseal development. AM. J. ROENTGENOL. & RAD. THERAPY, 1931, *25*, 91–94.
26. SUMMERFELDT, P., and BROWN, A., Morquio's disease. *Arch. Dis. Childhood*, 1936, *11*, 221–229.
27. ULLRICH, O. Nachtrag zur Arbeit "Ueber die Dysostosis multiplex (Typus Hurler) usw." *Ztschr. f. Kinderh.*, 1933, *55*, 470–471.

VOL. 46, NO. 3

UNUSUAL METASTATIC BONE LESIONS*

By RICHARD A. RENDICH, M.D., and ABRAHAM H. LEVY, M.D.
BROOKLYN, NEW YORK

IT IS more or less conceded that the skeletal system is derived from mesoderm and by a process of differentiation this mesoderm lays the future groundwork from which its separate structures develop. In general, the term differentiation connotes an orderly progress toward the normal in tissue development and by certain inherent and intangible forces, as properties of the individual cell, cortical hard bone, cancellous bone, endosteum, periosteum, osteoblasts and osteoclasts come into being and relation. If one accepts this pluripotential nature of these primitive cells, one should not be surprised to see what at times appears to be odd developments either in the pathological or deviations from the normal.

It is with this thought in mind that 6 cases of metastatic involvement are herewith presented which had certain gross features in common with primary malignant bone tumor. However, thorough clinical investigation and biopsy of the involved area confirm the diagnosis of metastatic carcinoma.

Metastatic carcinoma is either osteoblastic or osteolytic, there being no definite rule between the primary growth and the type of metastases. Although osseous metastases from carcinoma of the prostate are usually osteoplastic lesions, bone metastases are not always exclusively destructive or productive, for both types of metastasis may be present simultaneously in the same bone and associated with the same primary growth. The gross and roentgenological appearance of bone production or bone destruction is dependent upon the most predominant of these factors. Review of the literature discloses three hypotheses for new bone formation associated with secondary cancer. Briefly stated they are as follows:

1. New bone formation is secondary to circulatory disturbances produced by the metastatic lesions (von Reckinghausen, Courvoisier, Kaufmann, Handley).
2. New bone formation is of the nature of a foreign body or "defense reaction" to a foreign body (Assmann, Copeland).
3. The carcinoma cells themselves secrete a substance which stimulates osteogenesis (Axhausen).[1]

These authors appear to refer to the new bone formation of the osteoplastic type of metastases. However, there occasionally occurs an osteolytic lesion with cortical destruction and new bone formation laid down in the tumor tissue perpendicular to the shaft. In this latter type, the work of Brunschwig[1] and Brunschwig and Harmon[2] is applicable. In attempting to explain these unusual metastatic lesions we must accept the experimental and clinical investigations of this author who has most satisfactorily shown that lesions arising, or those which are deposited within the medullary cavity and extend through and beyond the cortex, elevate the periosteum before them thus acting as a stimulus to this membrane to lay down new bone in the form of trabeculae radiating at right angles to the cortex, resulting in the "sun burst" pattern on the roentgenogram and the associated reactive triangles at the margins of the extracortical portions of the involved bone—findings so generally associated with primary osteogenic sarcoma. A study of the so-called newly formed perpendicular bone lamellations about the cortex of an osteoblastic metastasis producing a subcortical lesion reveals that the new bone is in the form of fine closely applied trabeculae radiating at right angles from the cortex. The similarity in pattern of the new bone in specimens from metastatic lesions and in certain primary growths suggests that the mechanism

* From the Department of Roentgenology, Kings County Hospital, Department of Hospitals, New York City.

which leads to these findings is identical in both instances, i.e. periosteal elevation.

Many of the earlier writings, especially after the advent of roentgenology, would have us believe that the lines of distinction were closely drawn between the benign and malignant groups of bone lesions.[5] However, more recent literature is frank in confessing that such differentiation is difficult. Even the more experienced are sometimes perplexed, since they are often confronted with features which have been conceded as peculiar to certain forms of disease, that may also be found in other forms. The roentgenologist is often faced with a difficult task. The important features which he must determine are—the malignancy or benignancy of the lesion and secondly, whether the lesion is single or multiple. That these distinctions are not always easy is demonstrated in the cases to be presented. From these, it will be evident that a complete roentgenographic examination of the osseous system is essential and frequently several complete studies at intervals thereafter.

CASE REPORTS

CASE 1. J. H., aged forty, single, upon admission complained of pain and swelling of multiple small joints of the hands and feet. The onset of his illness was four months prior to admission. These symptoms gradually became worse. The most outstanding pulmonary complaint was a chronic cough which was moderately productive. There was no dyspnea or ankle edema. The past history was irrelevant except for pneumonia five years before, at which time he was confined to bed for about fourteen days.

Physical Examination. White male, ambulant but walking with difficulty due to stiffness of his joints. Cardiovascular system was negative. Lungs revealed a localized area of consolidation in the region of the right upper lung field posteriorly. The finger joints showed fusiform swelling, were stiff and the finger tips clubbed. Patient was continued under observation. The lung picture changed but slightly. Repeated sputum examinations (fifteen) were negative for the tubercle bacillus. The temperature ranged from 98.6 to 100° F.

Roentgen Findings. The chest revealed an area of consolidation of the right upper lobe with suggestion of a small destructive process in its mid portion, as compatible with a lung abscess (Fig. 1, *A*). The small bones of the hands disclosed quite marked pulmonary osteo-arthropathy with the usual pattern of ossifying periostitis (Fig. 1, *B*). The remainder of the osseous system revealed a marked degree of hypertrophic pulmonary osteo-arthropathy of the phalanges of the toes and along the shafts of all the long bones (Fig. 1, *C*).

The clinicians felt that from a clinical standpoint the entire picture did not fit well with a lung abscess. Bronchoscopy was performed but the findings were negative, except for moderate discharge from the right main stem bronchus. Lipiodol installation of the right chest demonstrated nonfilling of the bronchus leading to the consolidated area. Lung puncture was attempted twice but was found to be unsatisfactory since a specimen from the consolidated area was not obtained.

Patient was discharged from the hospital after a stay of about six months with a diagnosis of tumor of the lung with secondary destruction and associated marked hypertrophic pulmonary osteo-arthropathy. Treatment while in the hospital was mainly symptomatic. Two months later the patient was readmitted complaining of pain in the right hip at which time a lump was discovered in the region of the lower third of the right tibia, which was 2 inches in diameter and was very painful.

Roentgenographic studies of this area revealed a destructive lesion, corticomedullary in location, osteolytic in type, and possessing perpendicular bone lamellations with evidence of reactive triangles at the borders of the destructive lesion. Osteogenic sarcoma, lymphatic growth and lues were considered in the differential diagnosis (Fig. 1, *D*). Roentgen studies of the chest at this time showed no gross change in the infiltrative process of the right upper lobe. Special attention is called to the interval studies of the long bones which disclosed marked regression of the pulmonary osteo-arthropathy (Fig. 2, *A*). This was apparently spontaneous since the pulmonary pathology was not grossly altered and the medication was entirely symptomatic. Roentgenologically, the remainder of the osseous system at this time showed no other osteolytic lesions. Patient gradually became worse and prior to his death, which was four months after the second admission, he developed other metastatic foci—one to the proximal phalanx of the little finger of the right

FIG. 1. Case 1. *A*, examination of the chest at the time of admission revealed an area of consolidated lung, right upper lobe. *B*, soft tissue film demonstrating marked pulmonary osteo-arthropathy of the small bones of the left hand and radius. *C*, soft tissue film disclosing pulmonary osteo-arthropathy along the shafts of the long bones. *D*, corticomedullary osteolytic lesion with perpendicular newly formed bony lamellations extending into the adjacent soft tissues and evidence of reactive triangles at the borders of the destructive lesion.

hand and another to the outer end of the right clavicle. Roentgen studies revealed, at this time, practically complete absence of the proximal phalanx of the right little finger—the result of an osteolytic medullary metastatic lesion (Fig. 2, *B*). The outer end of the right clavicle was involved by a similar destructive process.

Biopsies of the bony lesions proved to be metastatic papillary carcinoma, Grade 2. The histopathological report on the specimen taken from the tibia was as follows: "Examinations of the material disclosed fragments of tissue made up of a papillary adenomatous growth; the cells lining the papillary growth are large in character with a considerable amount of pink staining protoplasm, many showing vacuolization. Certain areas present a markedly disorderly appearance; many of the nuclei are hyperchromatic; there is also evidence of mitosis; many areas show a considerable amount of necrotic cellular

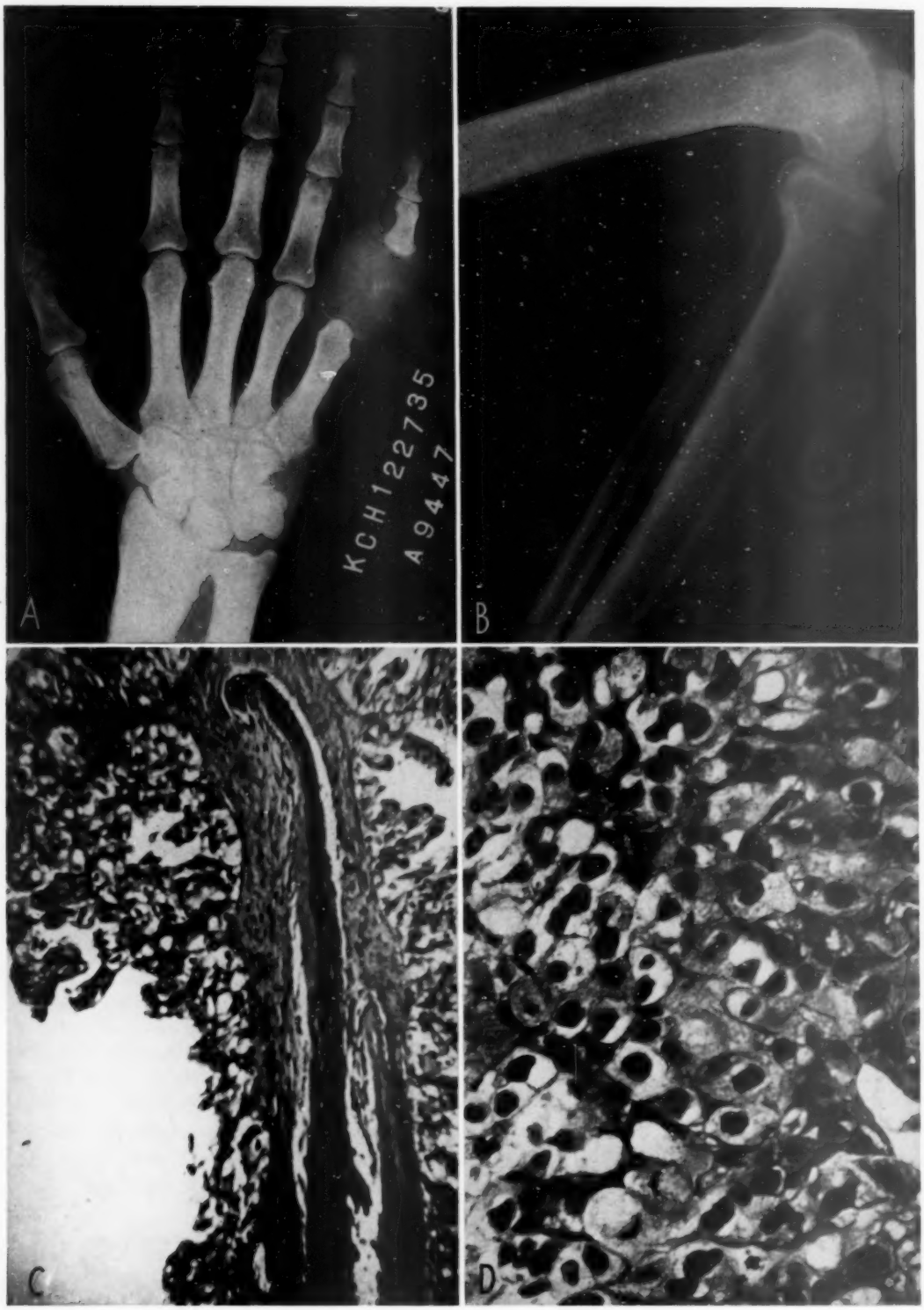


FIG. 2. Case 1. *A*, osteolytic medullary metastatic lesion, proximal phalanx little finger right hand. This lesion developed prior to the patient's death. Attention is called to complete disappearance of the pulmonary osteo-arthropathy about the fingers, but with retention at the distal end of the radius. *B*, almost complete

debris and serum. Diagnosis: Papillary carcinoma Grade 2—original focus probably lung (Fig. 2, *C* and *D*).*

Case II. M. K. was admitted with a chief complaint of swelling and pain in the right ankle for the past two months. This swelling had been increasing moderately of late. It had always been hard and walking caused exaggeration of his pain. He had a fracture of the upper third of his right tibia ten years before.

Physical Examination. Well developed white male, fifty-four years of age, ambulant, deformity of the right lower leg with a hard swelling 3 inches in diameter on the anterior aspect of the tibia. This mass was tender to the touch and mobility and flexion of the ankle were limited.

Roentgen Findings. The lower end of the right tibia revealed an osteolytic corticomedullary lesion with a reactive triangle at the margins of the invading bony growth together with perpendicular newly formed bone extending into the adjacent soft tissues (Fig. 3, *A*). This roentgen appearance was very similar to that noted in the previous case. The entire osseous system at this time revealed no other lesion. Examination of the chest disclosed a small irregular area of infiltration of the parenchymal substance springing from the left hilum, which at the time was not sufficiently characteristic to form a definite opinion but metastasis was considered as most likely. During the past three months, this lesion has assumed features even more significant of a nodular type of metastasis. Second examination of the osseous system after a stay in the hospital for six months still showed no evidence of other metastatic bony changes.

Biopsy from the tibia (Fig. 3, *B* and *C*) was reported as follows: "Section taken from bone which is made up of fibrous and osteoid tissue. Marked fibroblastic reaction is present which makes up the major portion of the stroma of the specimen. There are focal areas of myxomatoid tissue which are undoubtedly young connective tissue cells. Lying within the stroma are clusters of neoplastic cells which have a tendency towards alveolar formation; many of them show compression due to the surrounding desmoplasia. These neoplastic cells show round and fusiform outlines and are markedly hyperchromatic. There are also noted in several places large giant cells which are probably foreign body reaction cells. Several are very large in size and show bizarre nucleation. No actual calcified bony spicules are seen. However, there are noted areas of osteoid tissue. There is also evidence of chronic inflammatory reaction focally which is characterized by collections of lymphocytes. Pathological diagnosis: Metastatic adenocarcinoma, origin unknown.

Case III. R. F., female, white, aged forty-three, Italian. Thyroidectomy in 1935. Four years later a lump was noted in the supraclavicular region on the right side. Biopsy was done at another hospital and roentgen therapy administered. Shortly afterward, a lump was noted in the right thigh. Biopsy report from specimen obtained from this region revealed metastatic carcinoma of thyroid origin (Fig. 4, *A*). Roentgen report was that of a corticomedullary malignant lesion with perpendicular newly formed bone extending into the adjacent soft tissues. There were no other lesions demonstrable in the remainder of the skeletal system. Roentgen diagnosis, metastatic carcinoma.

Case IV. P. J., female, colored, aged sixty, whose chief complaint was inability to get about for the past six weeks. Stiffness in the right thigh for past several months. Roentgen findings disclosed a corticomedullary malignant lesion of the proximal third of the femur apparently metastatic in nature. The remainder of the osseous system was devoid of any other foci. Biopsy of the bone lesion revealed metastatic carcinoma probably originating from the gastrointestinal tract (Fig. 4, *B*).

Case V. H. C., white male, aged seventy-five. Patient had complained of pain in the back and right thigh for a long time. Physical examination revealed a lemon-sized, hard, nodular mass which was painful to the touch in the right lower quadrant of the abdomen above Poupart's ligament. Roentgen examination of the pelvis

* From Department of Pathology, Kings County Hospital, Dr. William Hala, Director.

regression of the pulmonary osteo-arthropathy of the long bones after an interval of eight months, apparently spontaneously. Soft tissue film. *C*, photomicrograph of biopsy from a section through the lesion of the distal end of right tibia showing anaplasia with marked variation in cellular structure. Many large atypical neoplastic cells are seen throughout with hyperchromatic nuclei—low power. *D*, high power of *C*.

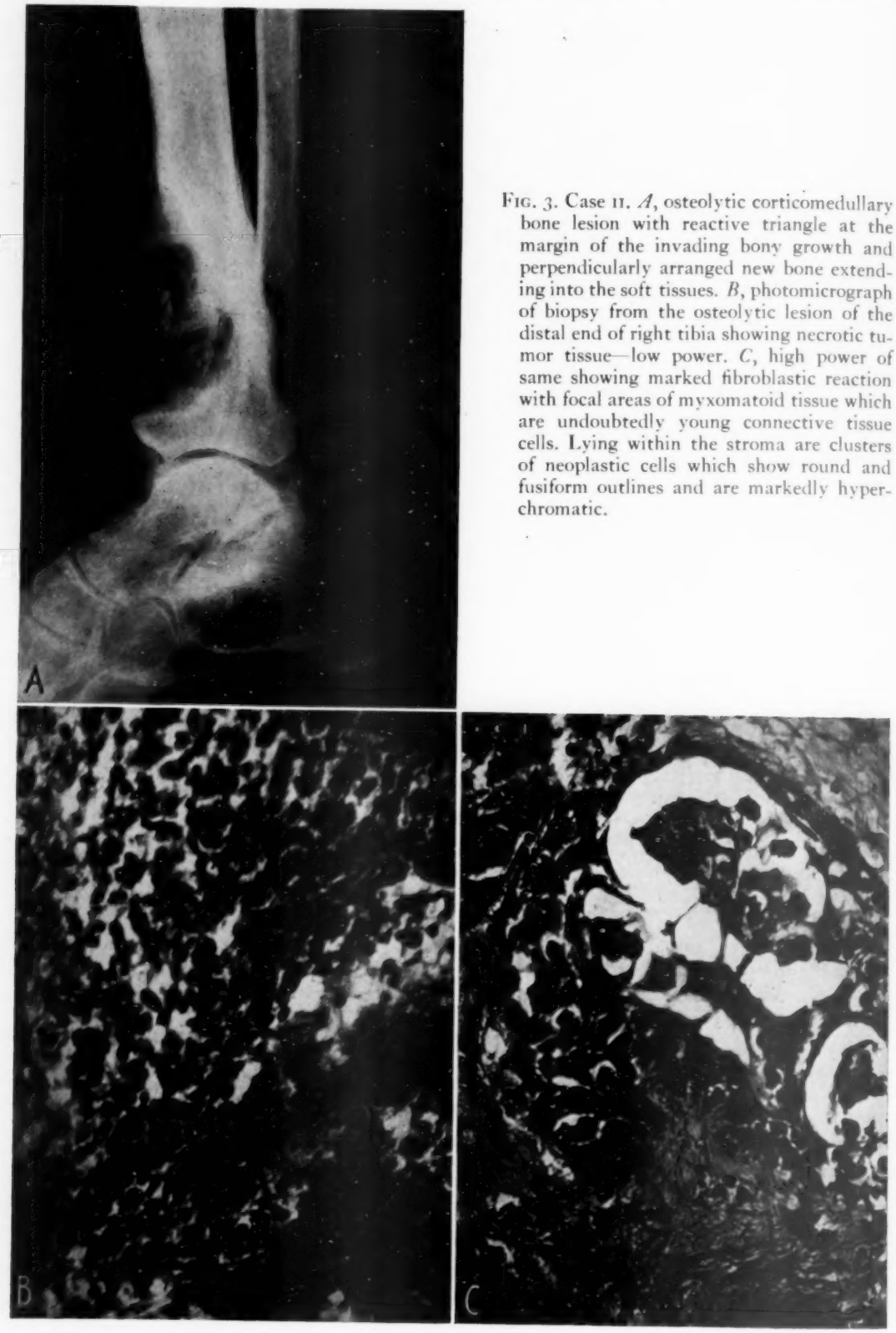


FIG. 3. Case 11. *A*, osteolytic corticomedullary bone lesion with reactive triangle at the margin of the invading bony growth and perpendicularly arranged new bone extending into the soft tissues. *B*, photomicrograph of biopsy from the osteolytic lesion of the distal end of right tibia showing necrotic tumor tissue—low power. *C*, high power of same showing marked fibroblastic reaction with focal areas of myxomatoid tissue which are undoubtedly young connective tissue cells. Lying within the stroma are clusters of neoplastic cells which show round and fusiform outlines and are markedly hyperchromatic.

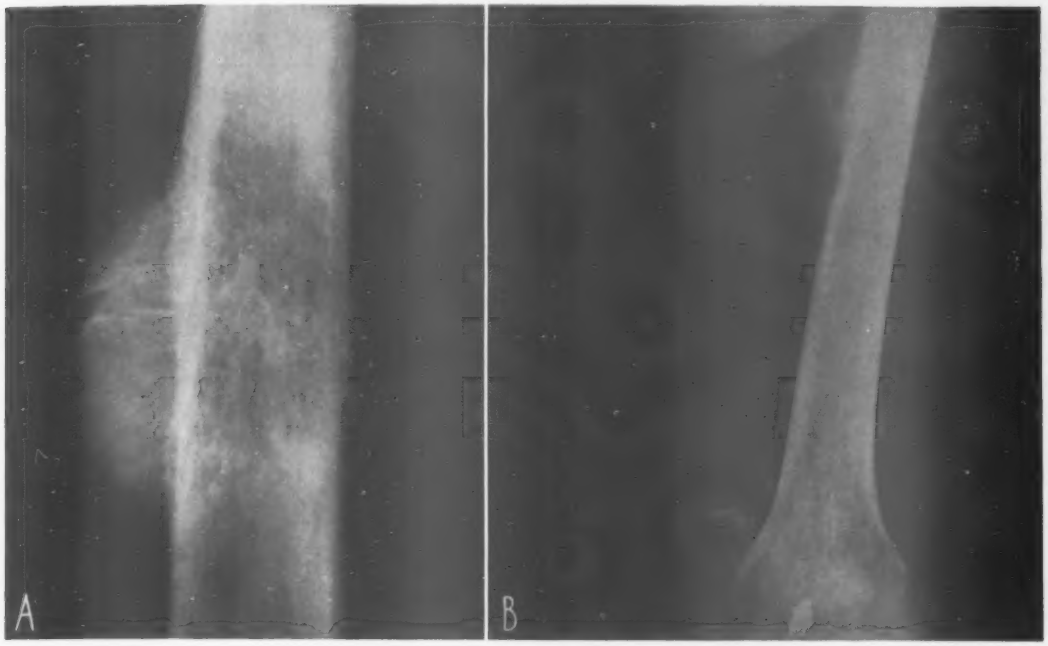


FIG. 4. *A*, Case III. Destructive corticomedullary bone lesion involving mid portion of right femur with newly formed perpendicular bony penetrations into the adjacent soft tissue. Roentgen diagnosis—metastatic carcinoma. Biopsy report—metastatic lesion from thyroid. *B*, Case IV. Corticomedullary malignant lesion of the right femur with perpendicular bony extension into the adjacent soft tissues. Roentgen diagnosis—metastatic carcinoma. Biopsy report—metastatic lesion from gastrointestinal tract.

FIG. 5. *A*, Case V. Corticomedullary destructive bony infiltration of the wing of right ilium with perpendicular new bone formation extending into the adjacent soft tissues. Roentgen and autopsy diagnosis was that of metastatic bone lesion. Autopsy revealed the primary site to be in prostate. *B*, Case VI. Osteolytic destructive corticomedullary lesion with marked invasion of the adjacent soft tissues on both the internal and external aspects of upper end of thigh. Roentgen diagnosis—metastatic lesion. Biopsy of the lesion revealed metastatic adenocarcinoma originating from the gastrointestinal tract.

disclosed a corticomedullary destructive bony infiltration of the wing of the right ilium with newly formed perpendicular bony lamellations extending into the adjacent soft tissues. The roentgen diagnosis at this time was metastatic bone lesion. Roentgen study of the osseous system disclosed another metastatic focus in the first lumbar vertebra. Patient died and the autopsy finding was that of adenocarcinoma of the prostate with metastasis to the iliac bone on the right side (Fig. 5, *A*).

CASE VI. A. M., white female, aged seventy-five, with complaint of pain and a mass in the left hip region for the past eighteen months. Physical examination revealed a large firm mass extending from the left hip to below the middle of the femur. The roentgenographic findings were those of an osteolytic destructive corticomedullary lesion with marked invasion of the adjacent soft tissues on both the internal and external aspects of the upper end of the thigh. The impression was that of a metastatic bone tumor. Roentgen examination of the remaining portion of the osseous system disclosed no other foci. Biopsy of the bone lesion revealed a metastatic adenocarcinoma originating from the gastrointestinal tract (Fig. 5, *B*).

SUMMARY AND CONCLUSIONS

Six cases of metastatic malignant disease are presented, unusual in the following features:

1. Destructive corticomedullary lesions with perpendicular newly formed bony lamellations extending into the adjacent soft tissues and reactive triangles, in contrast to the usual medullary purely centralized lesions.
2. In two of the cases the initial evidence of bony metastases occurred below the knee rather than proximal to it.
3. Spontaneous resolution of a marked degree of pulmonary osteo-arthropathy in the small bones of the hands and lower extremities.
4. The necessity of a thorough roentgenographic examination of the osseous system with repeated interval studies in any case of bone tumor in which the diagnosis is not definitely determined is emphasized.

REFERENCES

1. BRUNSCHWIG, A. Reaction of bone to invasion by carcinoma. *Surg., Gynec. & Obst.*, 1936, *63*, 273–282.
2. BRUNSCHWIG, A., and HARMON, P. H. Studies in bone sarcoma: experimental and pathological study of rôle of periosteum in formation of bone in various primary bone tumors. *Surg., Gynec. & Obst.*, 1935, *60*, 30–40.
3. GESCHICKTER, C. F. Osteogenic sarcoma. *Arch. Surg.*, 1932, *24*, 602–659.
4. PHILLIPS, C. Osteogenic sarcoma: its pathologic characteristics. *Radiology*, 1935, *24*, 728–731.
5. WILSON, R. T. Osteogenic sarcoma: roentgenologic characteristics. *Radiology*, 1935, *24*, 708–714.

MULTIPLE BONY LESIONS SUGGESTING MYELOMA IN A PRE-COLUMBIAN INDIAN AGED TEN YEARS

By GEORGE D. WILLIAMS,* WILLIAM A. RITCHIE† *and* PAUL F. TITTERINGTON‡

THE skeleton to be described was found accidentally in July, 1933, by Mr. Frank Limpert, who was grading a hillside for a lawn. The site of the discovery is a side of a high narrow sand ridge formed by the post-Pleistocene dissection of glacially filled Irondequoit Bay, the ancient course of the Genesee River, opening from Lake Ontario, about one and one-half miles east of Rochester, New York. Mr. Limpert, accompanied by his wife and several boys, uncovered the flexed skeleton 2 feet below the surface and directly beneath the roots of an oak tree of about 1 foot diameter.

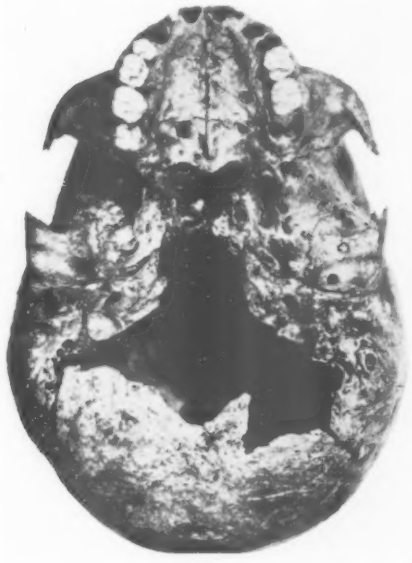


FIG. 1. Base of skull showing lesions.*

No mortuary offerings were observed, but several flint points and a few ovate pebbles, grooved about the long axis and believed to be bolas stones, were found later in the general vicinity of the burial by Mr. Limpert and his helpers.

The find was reported to the Rochester Museum of Arts and Sciences and Director A. C. Parker and Mr. Donald Ritchie visited the site. Unfortunately, by that time the skeleton had been completely removed. Close examination of the grave fossa and of test pits sunk in the adjacent area produced nothing. Later, one of the authors (W. A. R.) intensively test-pitted the vicinity of the slope and summit of the sand ridge but found only a piece of local fossiliferous hematite (Clinton iron ore), worked as a paint stone, which lay on the surface 40 feet south of the grave.

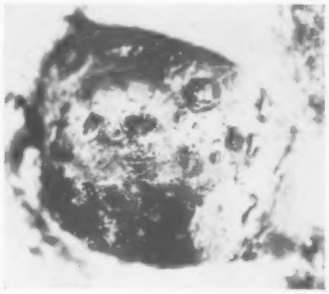


FIG. 2. Lesions in left orbit.

In the absence of directly associated cultural criteria, it is impossible definitely to attribute the burial to any one of the seven pre-Columbian and pre-Iroquoian occupations known in western New York. The industrial material, viz., the flint points, bolas stones and paint stone may antedate or post-date the burial, but it seems rather more probable that the total congeries belongs to a small camp site, many of which exist about the bay. The flint points were taken away by their finders and no adequate description of them is obtainable. The paint stone is in the inventory of virtually every New York culture. The bolas stones, however, are known lithic components of only four

* All roentgenograms by P. F. Titterington.

* From the Department of Anatomy, School of Medicine, Washington University, St. Louis. Mo.
† From the Division of Archaeology of the Rochester Museum of Arts and Sciences, Rochester, N. Y.
‡ From the Department of Radiology, School of Medicine, St. Louis University.

cultures of western New York, viz., (1) the Middlesex and (2) Point Peninsula Foci of the Vine Valley Aspect, (3) the New York Focus of the Hopewellian Phase and (4) the

FIG. 3. Lesions in left orbit and in left frontal bone.

Canandaigua Focus of the Owasco Aspect.* Burials associated with the first three cultures are usually provided with grave

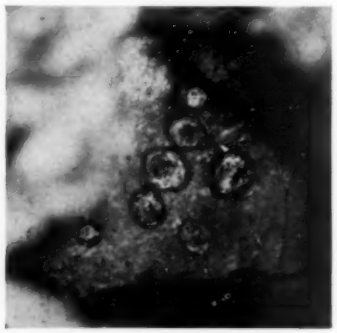


FIG. 4. Lesions on inner table of frontal bone.

goods, while the Owasco burials rarely contain them. This culture is the most recent of the four named, probably being dominant in the thirteenth century. It is a semi-sedentary, horticultural complex and is known to occur in a number of Irondequoit camp sites. The archaeologist among the authors suggests provisional association of the skeleton with the Canandaigua Focus, Owasco Aspect (see Ritchie[5]).

The skeleton is that of a child whose dental age is ten years. The condition of the epiphyses of the long bones and the size

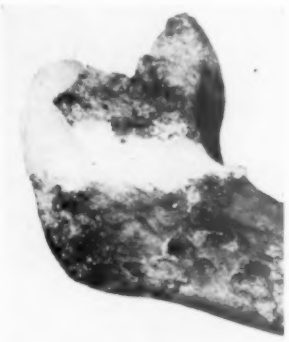


FIG. 5. Lesions on medial surface of left side of mandible.

of the bones in general are in harmony with this aging. The skull shows low brachycephaly (cranial index, 81.2), low, wide

FIG. 6. Ribs, left calcaneus, left ischium, showing lesions.

nasal bones and bridge, guttered lower borders of the piriform aperture and moderate prognathism. Except for the pathological conditions found, the skeleton in general is only remarkable for the presence of platymeria and platycnemia, which are anteroposterior and lateral flattenings of the upper femur and the middle tibia respectively, and are found almost constantly

* For a summary of these cultures see Ritchie.[6]

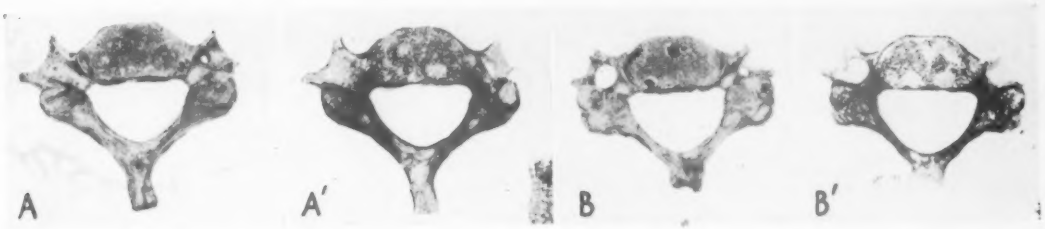


Fig. 7. Vertebrae, contrasting photographs, *A*, *B*, with roentgenograms, *A'*, *B'*.

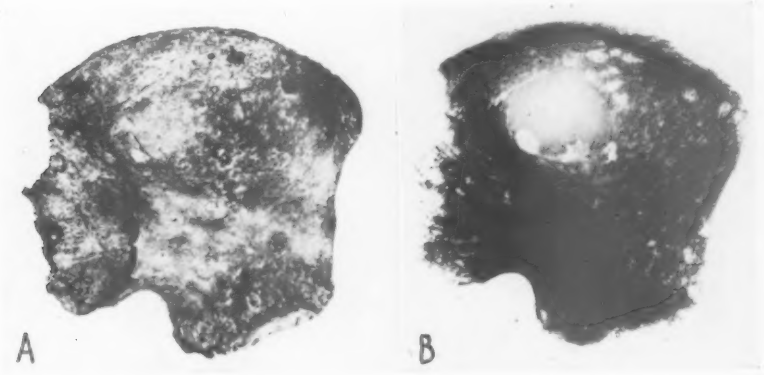


Fig. 8. Left ilium, photograph, *A*, and roentgenogram, *B*.

Fig. 9. Left femur showing few lesions.

Fig. 10. Right tibia; note multiple lesions in film, *B*.

Fig. 11. Right fibula; note multiple lesions in film, *B*.

in ancient American Indian bones. As to the relative completeness of the skeleton, one of the authors (W. A. R.) notes that other skeletons from similar, but probably

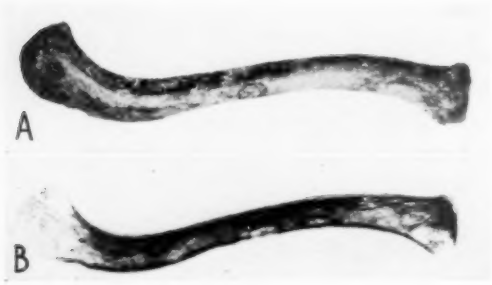


FIG. 12. Left clavicle, photograph, *A* and roentgenogram, *B*.

older, sand graves elsewhere on the bay, were in an advanced state of disintegration. This is further reason for suspecting an Owasco provenience for the burial. For examination, then, is presented the fairly

FIG. 13. Left humerus, exhibiting multiple lesions in roentgenogram, *B*.

complete skeleton of a child of about ten years, probably male, almost certainly American Indian and presumably dating from about the thirteenth century, A. D.

A first quick glance over the skeleton notes the wide distribution of punched-out

FIG. 14. Left radius, showing multiple lesions in roentgenogram, *B*.

FIG. 15. Left ulna, showing few lesions.

lesions from 3 to 10 mm. in diameter in almost every bone. The infratemporal region, the base of the skull, the palate and the left orbit show them, as does the internal surface of the body of the left side of the mandible. No ribs and no vertebrae are free from them. The component parts of the hip bones and the scapulae are next most affected, and the long bones in general least of all, although they are by no means sound. The sternum is missing from the skeleton. The widespread invasion of the bones by the lesions has not produced either fracture or deformity.

That the condition is probably that designated by the terms "multiple myeloma" or "myeloma" (Ewing[2]) is demonstrated by the classical descriptions of that condition here presented:

> The lesions are characteristically multiple and, in general, confined to the location of the red marrow, and thus in the roentgenogram may be termed typically central. The tumors are bone destructive and show in the pictures as rounded punched-out areas varying from the size of a pea to that of an orange. . . . When the long bones are affected, they show, in the early stages, either the multiple punched-out areas, or more rarely an expanded cystic change. —Geschickter and Copeland.[3]

> The tumor begins in the marrow and as it grows causes destruction of the surrounding bone. . . . As growth continues, rather sharply defined punched-out areas are produced in multiple areas in the affected bones. The finding of multiple punched-out areas scattered through one or more bones, with or without bony deformity and enlargement but without neoplastic bone formation, together with biopsy examination . . . and the occurrence of Bence-Jones albumose in the urine, are sufficient to establish the diagnosis.—Stout.[7]

The photographs and reproductions of roentgenograms give a better description of the pathological process in the skeleton of the Indian child than words will do. Where possible roentgenograms are shown beside photographs of the bones. From these juxtaposed pictures the presence of lesions within the bones (in the marrow cavity, shown in the roentgenograms) and their absence in many cases on the outside of the bones (in the photographs), is demonstrated. The marrow origin of the lesions is obvious.

The first interesting point about this case is that it occurs in a pre-Columbian American Indian. Geschickter and Copeland[3] believe that the disease occurs in all races and report it in whites, Negroes and Chinese. One of the co-authors of this paper reported in this Journal (Ritchie and Warren[4]) the first recorded instance in a pre-Columbian American Indian.*

The second point that makes this case unique is the age of the subject. Cases so far reported in children give ages from two to twelve and one-half years. These are not certainly accepted as multiple myelomas by Christopher[1] or by Geschickter and Copeland.[3] We can only state that, although it is impossible to prove the diagnosis by biopsy showing cystic tumor cells and the presence of Bence-Jones protein in the urine, we believe that the nature and distribution of the lesions point to a diagnosis of multiple myeloma in this skeleton of a thirteenth century American Indian aged about ten years.

REFERENCES

1. Christopher, F. A. Textbook of Surgery. W. B. Saunders Co., Philadelphia, 1936.
2. Ewing, J. Neoplastic Diseases. Fourth edition. W. B. Saunders Co., Philadelphia, 1940.
3. Geschickter, C. F., and Copeland, M. M. Tumors of Bone. American Journal of Cancer, New York, 1936.
4. Ritchie, W. A., and Warren, S. L. Occurrence of multiple bony lesions suggesting myeloma in the skeleton of a pre-Columbian Indian. Am. J. Roentgenol. & Rad. Therapy, 1932, *28*, 622–628.
5. Ritchie, W. A. A Prehistoric Fortified Village Site at Canandaigua, Ontario Co., New York. Research Records, Rochester Museum of Arts and Sciences, 1936, No. 3.
6. Ritchie, W. A. A perspective of Northeastern archaeology. *American Antiquity*, 1938, *4*, 94–112.
7. Stout, A. P. Human Cancer. Lea & Febiger, Philadelphia, 1932.

* The subject in that case was senile. His archaeological horizon was probably that of the ninth century, A. D.

PROTHROMBIN FORMATION FOLLOWING INJURY OF BONE MARROW BY ROENTGEN RAYS*†

By W. A. BARNES, M.D.
NEW YORK, NEW YORK

THE development of quantitative methods for the determination of prothrombin activity[12,13] almost coincidental with the discovery of vitamin K[1,4] has heightened interest in the blood clotting mechanism, and in problems relating to the sites of origin of prothrombin.

The investigations of the past few years have established the liver as the organ chiefly responsible for the formation of prothrombin. While earlier investigation suggested that formed elements of the blood and bone marrow were important in the elaboration of prothrombin,[8] little mention has been made recently concerning the relationship of bone marrow to prothrombin.

The experiments to be described were undertaken to investigate by means of roentgen irradiation the rôle of the bone marrow in the formation of prothrombin. Other investigators injured the bone marrow with benzol;[8] this substance also injures the liver. The liver cells are relatively resistant to roentgen rays, while marrow cells are among the most susceptible. By destruction of the bone marrow roentgen rays not only produce leukopenia, but Duke[6] showed that large doses of roentgen rays reduce the number of circulating platelets.

REVIEW OF LITERATURE

Morawitz[10] found that aqueous extracts of the platelets, after the addition of calcium, caused a solution of fibrinogen to clot and concluded that platelets contain prothrombin in large amounts. His findings were confirmed by Bayne-Jones[3] and by Howell,[7] who showed also that prothrombin is present free in blood plasma and lymph. Hurwitz and Drinker[8] produced aplasia of the bone marrow and low platelet counts in dogs by the injection of benzol. They found a fall of the prothrombin level associated with a decreased number of platelets. However, they did not produce an extremely low prothrombin level, indicating a source of prothrombin in addition to the platelets. From perfusion experiments on bone marrow Drinker and Drinker[5] concluded that megakaryocytes were the source, and platelets the carriers of prothrombin. Perfusion experiments of the spleen showed no prothrombin formation there, and perfusion experiments of the liver indicated very slight prothrombin formation in this organ.

As early as 1905 Nolf[11] found that extirpation of the liver of dogs caused a gradual diminution and final disappearance of coagulation in the blood of these animals. More recent investigations have pointed toward the liver as the chief source of prothrombin. Warner, Brinkhous and Smith[13] observed in dogs that after prolonged exposure to chloroform the blood prothrombin level decreased sharply. A similar drop was observed in dogs poisoned with phosphorus. There was no change in the platelet count. At autopsy extensive damage of the liver cells was found in both cases, and no significant lesions in the bone marrow. Following partial hepatectomy in rats, Warner[14] noted a conspicuous decrease of plasma prothrombin within a few hours. Other investigators[2,15] have observed a continuous fall in the plasma prothrombin of dogs following hepatectomy. Lord[9] demonstrated that trauma to the liver (gentle massage) caused a conspicuous fall of the plasma prothrombin.

MATERIAL AND METHODS

Mice, rats, rabbits and a dog were used. In all animals except mice the prothrombin

* From the Departments of Pathology and Surgery, Cornell University Medical College and the New York Hospital.
† This study was supported by grants from The Anna Fuller Fund, the Lady Tata Memorial Trust, and by a Fund for the Study of Leukemia.

level was established before treatment, in the experimental as well as in a control animal. In mice, because of the small volume of blood available, pooled blood of animals of the same stock and age was used.

The prothrombin level was determined by the method of Warner, Brinkhous and Smith,[13] performed by Miss Carol Ranges and Miss Florence Stevens of the Department of Surgery of the New York Hospital and Cornell University Medical College.

Irradiation was done by Miss Ruth Pidgeon of the Department of Radiology. The usual factors were: 200 kv., 15 ma., 25 cm., 3 mm. Al, 320 r per min. In the experiments illustrated in Charts II, III, and IV, general body irradiation was used except where stated otherwise: 200 kv., 15 ma., 150 cm., 1 mm. Al, 7.5 r per min.

EXPERIMENTAL RESULTS

Table 1 shows that there were no consistent changes in prothrombin level from one to six days following total irradiation of 48 mice and 4 rats with as much as 8,000 r. Microscopic examination of the bone marrow of many of these irradiated animals showed almost complete absence of hematopoietic cells. However, there were numerous platelets in blood smears even four days after irradiation with 8,000 r.

The effect on plasma prothrombin and leukocytes of total irradiation of Rabbit No. 1 (1,200 grams) with two large doses of roentgen rays is shown in Chart 1. The plasma prothrombin increased slightly after a total of 6,720 r. The platelets numbered 336,000 per cu. mm. on the day the animal was killed, although the bone marrow was aplastic.

TABLE I

EFFECT ON PROTHROMBIN LEVEL OF TOTAL IRRADIATION OF MICE AND RATS

Experiment No.	Number of Animals	Dose of Roentgen Rays (r)	Killed—Days after Irradiation	Prothrombin Per Cent Normal
1	5	640	3	100
	4	640	6	91
	4	—	—	100
2	4	800	2	137
	3	800	5	137
	3	—	—	100
3	7	960	5	110
	8	—	—	100
4	7	3,200	4	100
	7	—	—	100
5	1	Before irradiation	—	100
		3,200	3	92
	1	Before irradiation	—	100
		3,200	3	116
	1	—	—	100
6	7	6,000	1	100
	7	6,000	3	74
	7	—	—	100
7	6	8,000	4	71
	6	—	—	100
8	1	Before irradiation	—	100
		8,000	3	100
	1	Before irradiation	—	100
		8,000	3	100

Rats were used in Experiments 5 and 8; in the other experiments, mice.

These experiments indicate that large doses of roentgen rays directed at the entire body of animals fail to change consistently the plasma prothrombin level from one to five days after irradiation. Although the bone marrow was almost completely aplastic after a few days, circulating platelets persisted to the day of death. Attempts were made, therefore, to reduce the number of platelets by protracted irradiation.

In similar experiments Rabbits No. 2 and 3, two adult rabbits weighing 3,030 grams and 2,880 grams respectively received a total of 1,250 and 1,175 r respectively during twenty-six days. The effect on the prothrombin and blood elements is shown in Charts III and IV.

The numbers of circulating platelets were

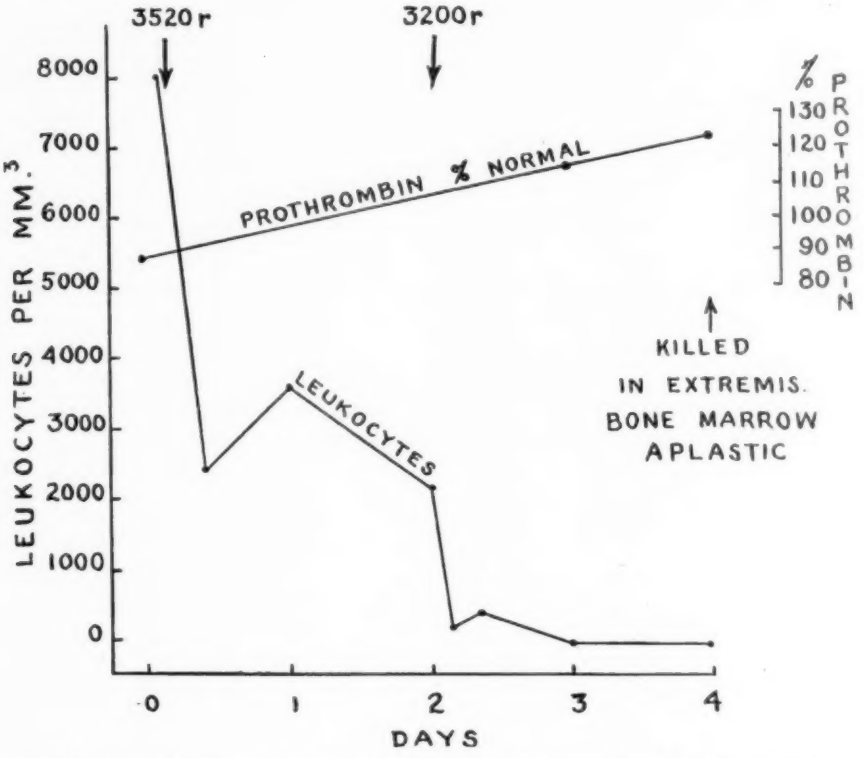


CHART I. Effect on plasma prothrombin and leukocytes of total irradiation of Rabbit No. 1.

Chart II shows the effect of long continued irradiation on plasma prothrombin and blood cellular elements of a dog. The liver of this animal was shielded from the direct action of roentgen rays except during the last irradiation. While the numbers of leukocytes and platelets decreased during the course of the experiment, the plasma prothrombin level remained unchanged even after 2,600 r in a single dose had been delivered to the entire body. Microscopic examination of the liver showed no conspicuous change. Both the vertebral and femoral bone marrow was almost completely devoid of hematopoietic cells.

conspicuously lowered following repeated doses of roentgen rays and rose rapidly after treatment was suspended (Charts III and IV). Despite the wide fluctuation in platelet counts (from 37,000 to 746,000 per cu. mm.), the plasma prothrombin did not vary significantly.

The effect on plasma prothrombin of irradiation of the region of the liver is still under investigation. Preliminary experiments indicate that single large doses of roentgen rays (6,400 r) directed to the region of the liver or to the entire body of rabbits pro-

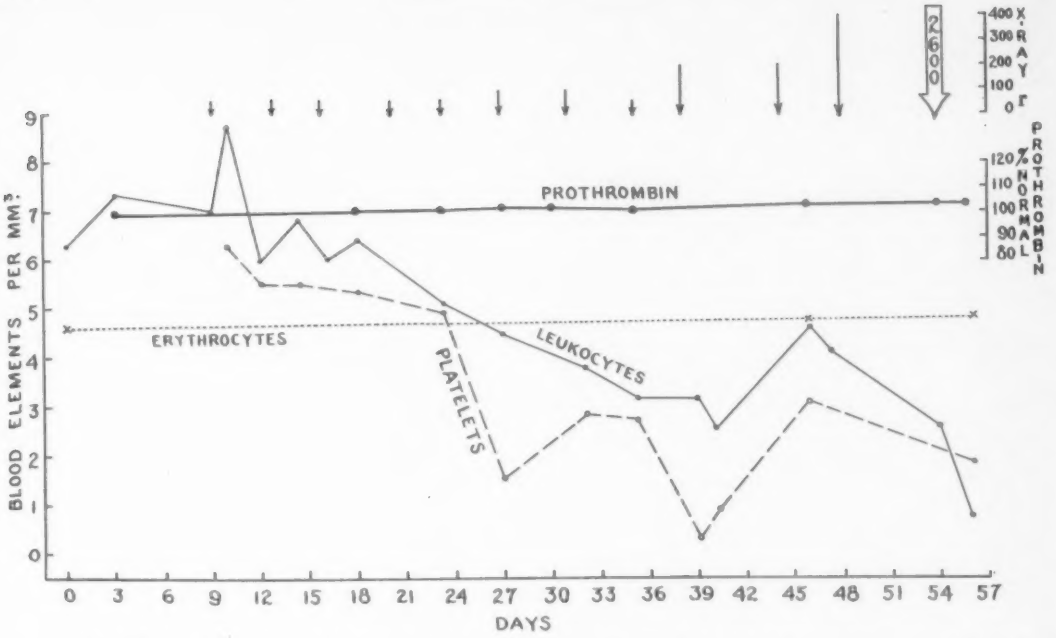


Chart II. Effect of protracted irradiation on formed elements of the blood and prothrombin of a dog.

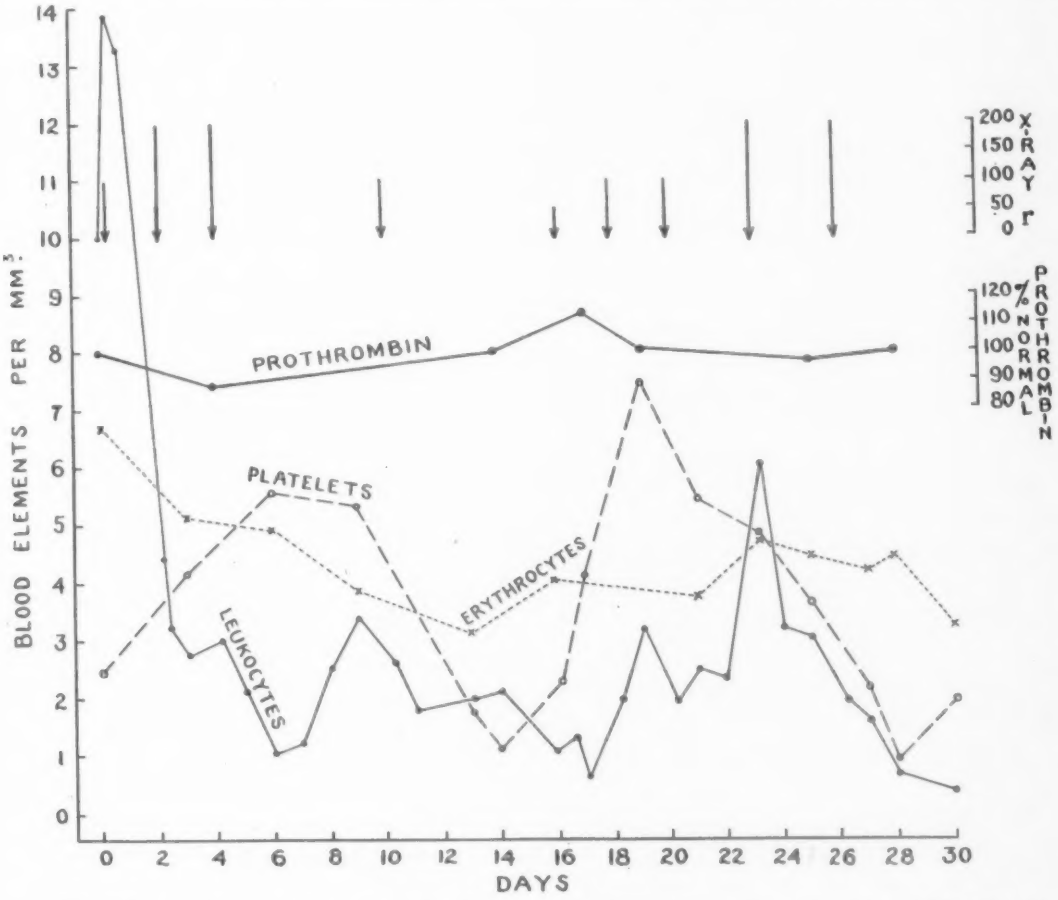


Chart III. Effect on formed elements of the blood and prothrombin of total irradiation of Rabbit No. 2.

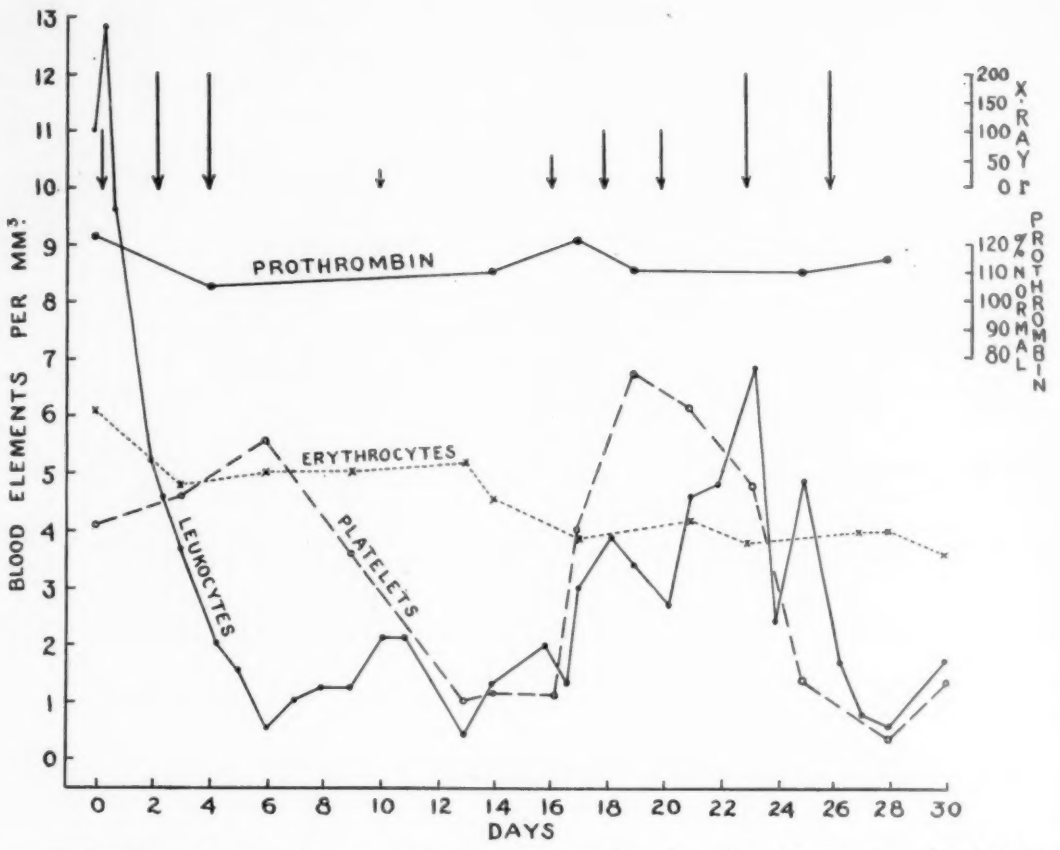


CHART IV. Effect on formed elements of the blood and prothrombin of total irradiation of Rabbit No. 3.

duce a temporary decrease of plasma prothrombin during several hours with no significant change from one to five days later.

SUMMARY

Total irradiation of 48 mice, 4 rats and a rabbit with moderate and large single doses of roentgen rays produced no significant alteration in prothrombin level during a period of from one to six days. The bone marrow of these animals was almost aplastic, although the blood contained numerous platelets.

Long continued irradiation of a dog and 2 rabbits produced no significant change in prothrombin level of the blood, although the number of platelets and the leukocyte counts were conspicuously lowered.

CONCLUSION

The plasma prothrombin level is not altered by profound depression of the bone marrow with severe leukopenia and thrombocytopenia resulting from roentgen irradiation.

Messrs. S. M. Bulkley, W. R. Eastman, W. T. Hudspeth and W. T. Mosenthal assisted in this study.

REFERENCES

1. ALMQUIST, H. J., and STOKSTAD, E. L. R. Hemorrhagic chick disease of dietary origin. *J. Biol. Chem.*, 1935, *111*, 105–113. *Abstr.* Dietary haemorrhagic disease in chicks. *Nature, London*, 1935, *136*, 31.
2. ANDRUS, W. DEW., LORD, J. W., JR., and MOORE, R. A. Effect of hepatectomy on plasma prothrombin and utilization of vitamin K. *Surgery*, 1939, *6*, 899–900.
3. BAYNE-JONES, S. The presence of prothrombin and thrombo-plastin in the blood platelets. *Am. J. Physiol.*, 1912–1913, *30*, 74–79.
4. DAM, H., and SCHÖNHEYDER, F. Deficiency disease in chicks resembling scurvy. *Biochem. J.*, 1934, *28*, 1355–1359.

5. Drinker, C. K., and Drinker, Katherine R. The bone marrow as a source of prothrombin. *Am. J. Physiol.*, 1916, *41*, 5–20.
6. Duke, W. W. Variation in platelet count, its causes and clinical significance. *J. Am. M. Ass.*, 1915, *65*, 1600–1607.
7. Howell, W. H. Prothrombin. *Am. J. Physiol.*, 1914, *35*, 474–482.
Howell, W. H. Coagulation of lymph. *Am. J. Physiol.*, 1914, *35*, 483–491.
8. Hurwitz, S. H., and Drinker, C. K. Factors of coagulation in experimental aplastic anemia of benzol poisoning, with special reference to origin of prothrombin. *J. Exper. Med.*, 1915, *21*, 401–424.
9. Lord, J. W., Jr. Effect of trauma to liver on plasma prothrombin; experimental study. *Surgery*, 1939, *6*, 896–898.
10. Morawitz, P. Beiträge zur Kenntnis der Blutgerinnung. *Beitr. z. chem. Phys. u. Path.*, 1903, *4*, 381–420; 1904, *5*, 133–141. Also, *Deutsches Arch. f. klin. Med.*, 1903–1904, *79*, 1–28; 215–233.
11. Nolf, P. Des modifications de la coagulation du sang chez le chien après extirpation du foie. *Arch. internat. de physiol.*, 1905–1906, *3*, 1–43.
12. Quick, A. J. Prothrombin in hemophilia and in obstructive jaundice. *J. Biol. Chem.*, 1935, *109*, lxxiii–lxxiv.
13. Warner, E. D., Brinkhous, K. M., and Smith, H. P. Quantitative study on blood clotting; prothrombin fluctuations under experimental conditions. *Am. J. Physiol.*, 1936, *114*, 667–675.
14. Warner, E. D. Plasma prothrombin; effect of partial hepatectomy. *J. Exper. Med.*, 1938, *68*, 831–835.
15. Warren, R., and Rhoads, J. E. Hepatic origin of plasma-thrombin observations after total hepatectomy in dog. *Am. J. M. Sc.*, 1939, *198*, 193–197.

THE USE OF IODIZED OIL IN ROENTGENOGRAPHY
WITH ANIMAL EXPERIMENTATION

By THOMAS ANDERSON HARTGRAVES, M.D., F.A.C.R.
The Lois Grunow Memorial Clinic
PHOENIX, ARIZONA

IODIZED oils are fixed compounds of iodine with some bland vegetable oil or their esters. They belong to a group of compounds known as halogenated oils which are fixed compounds of either iodine or bromine. All of these halogenated oils are radiopaque. No attempt is made here to evaluate the qualities of the various oils. It was thought best, however, to use only one of the products as long as it proved satisfactory. Accordingly, lipiodol (LaFay) was selected from among several easily obtainable products and this oil was used in all roentgenograms of patients and in all animal experiments reported here. Lipiodol is a fixed compound of iodine with poppy-seed oil containing 40 per cent iodine by weight, the iodine entering into the molecule of the combination. It must be remembered that when lipiodol is exposed to air, light, high temperature or humidity some of the iodine may be liberated from the compound and dissolve in the oil. This produces a slightly brownish color and any product showing this discoloration should be rejected for use as it may be irritating to some tissues.

The history of halogenated oils in roentgenography began in 1922 when their radiopaque quality was accidentally discovered by two Frenchmen, Forestier and Sicard,[2] although in America, Waters, Bayne-Jones and Rowntree[17] had carried out animal experimentation on the subject and reported their work in 1917. Following much pioneer work by Forestier and Sicard the halogenated oils rapidly assumed a definite place in roentgenography throughout the world. In this country these radiopaque substances were introduced and used by various authorities, among whom may be mentioned Proetz,[9] MacCready,[6] Fraser[3] and Goodyear.[4] Proetz, especially, deserves mention for his pioneer work in the use of these radiopaque oils for paranasal sinus diagnosis by his well known displacement method of injection. These men and others carried on their work with much enthusiasm in the middle 1920s, and from that time until the present the use of halogenated radiopaque oils in roentgenography has become so widespread that they are now in daily demand in almost every roentgenologist's office throughout the country. Methods of use have been simplified but have not yet become standardized in some diagnostic procedures.

The work of Proetz resulted in a more or less standardization of the technique in the use of radiopaque oils in paranasal sinus diagnosis, while Sante[11] and others have aided in making possible a more or less standardized technique for the use of iodized oils in roentgenography of the chest. The visualization of the pathology of bronchiectasis has become a common practice since the advent of iodized oils (Fig. 1, *A* and *B*). The visualization of many other pathological conditions in the chest is also enhanced or made possible by this means.

These iodized oils may also be used to demonstrate accurately various complicated sinus tracts. In demonstrating such sinus tracts by injecting iodized oil it is important that all outside openings be firmly closed in order that the somewhat viscous fluid can be made to fill and distend every portion of the tract (Figs. 2 and 3). It is best to inject these sinus tracts under roentgenoscopic control since blood vessels may be injected if they are open or unusually permeable.

In cholecystectomy it has been demonstrated that cholangiography with iodized oil is a valuable adjunct and obviates the necessity of exploration of the common bile

duct (Fig. 4). This procedure is thoroughly described by Sweek, Hartgraves and Williams[13] in a recent article. They describe how this may be carried out to the best advantage on the operating table and show its value in avoidance of postoperative shock and other dangerous and unpleasant postoperative conditions.

roentgenographic laboratories where roentgenoscopic control cannot be had. He injects lipiodol 2 cc. at a time, making a film after each 2 cc. of injection. Randall[10] describes a series of 600 hysterosalpingographies paralleled by a like number of Rubin insufflation tests. The results of his series indicates that the value of the two

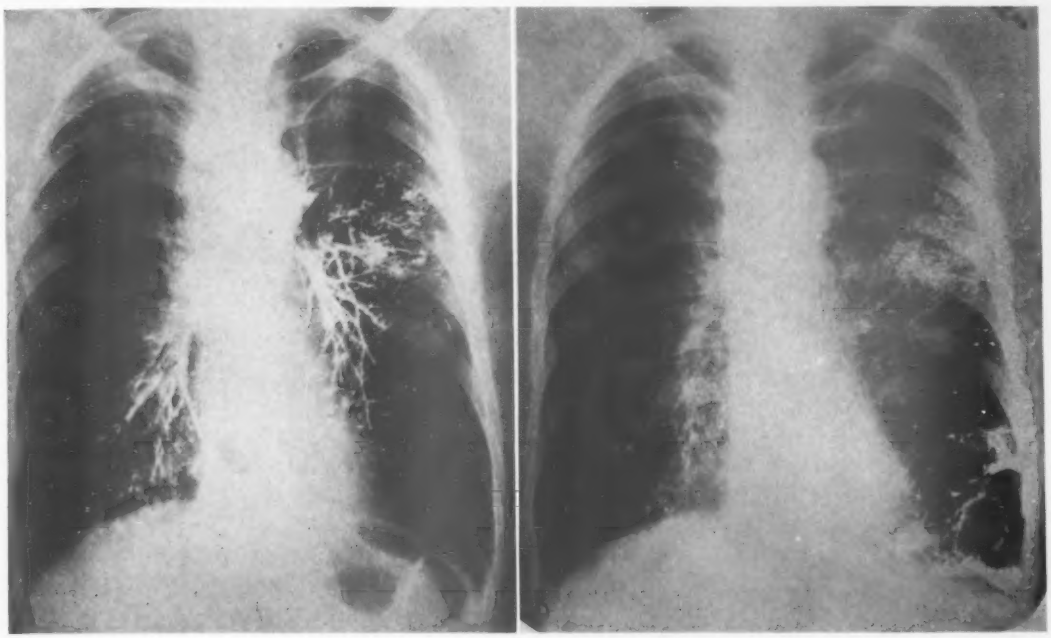


Fig. 1. Chest roentgenogram with lipiodol. *A*, showing bronchiectatic cavities near hilum of left lung; *B*, showing that large area with absence of lung markings in left costophrenic angle is in reality emphysematous lung tissue. A small amount of lipiodol was injected into lower portion of lung through the chest wall with a needle and syringe.

The use of iodized oil in spinal cord and spinal column pathology is a valuable diagnostic guide. It is perhaps well for the roentgenologist to carry out this procedure only in cooperation with a well qualified neurologist.

The use of iodized oil in hysterosalpingography has been described by so many writers that it is impossible to mention all. Some of the more recent articles are of special interest. Titus,[14] with Hyams, describes the use of hysterosalpingography in the practical aspects of sterility and compares it with the Rubin insufflation test. In this article Hyams suggests a method of procedure that might be preferable in methods is very nearly the same. Kleitsman and Haldre[5] describe a method which they call "salpingeurysis." In their method it is necessary for the patient to have a long period of observation—twenty-four to forty-eight hours—with a series of films. They claim by their method 40.9 per cent of successful production of tubal patency in women previously sterile. Various writers differ widely in their ideas of procedure. Formerly most writers specified that not more than a certain amount of oil must be injected (from 3 or 4 to 10 cc.), and that the careful measurement of the pressure was of great importance (not over 200 mm. Hg). More recently it has been stated by

some authorities that the amount of oil necessary may vary from 5 to 30 cc. and that the exact measurement of the amount of pressure used is of very little practical importance.[5,8] Other authorities, as mentioned above, insist upon a long period of observation following the injection and numerous roentgenograms, but this is countered by another writer who claims that a bimanual pelvic examination, made immediately after the first roentgenogram, makes it possible for a second roentgenogram to give practically all the information obtained by the long period of observation.[15]

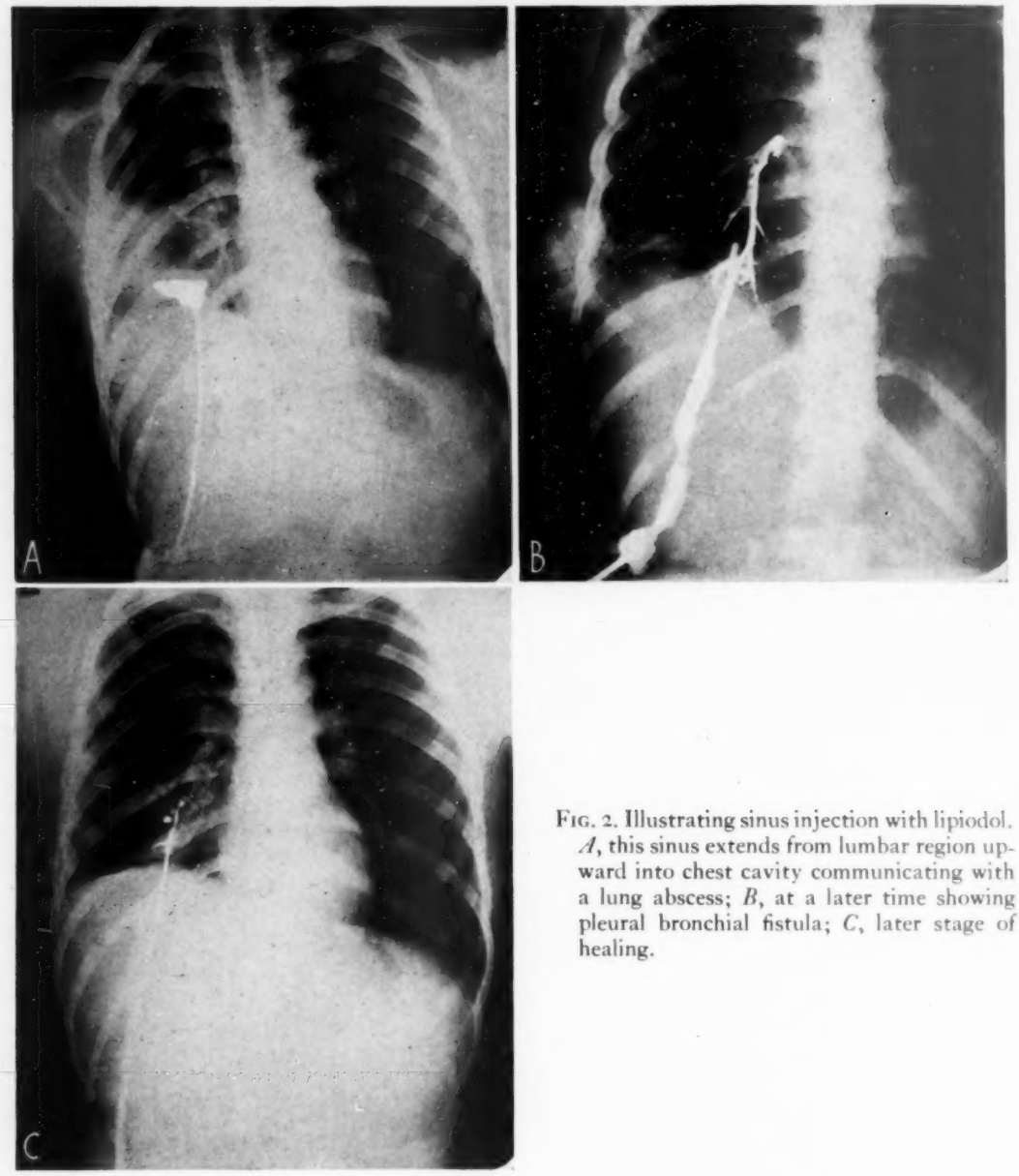


FIG. 2. Illustrating sinus injection with lipiodol. *A*, this sinus extends from lumbar region upward into chest cavity communicating with a lung abscess; *B*, at a later time showing pleural bronchial fistula; *C*, later stage of healing.

From all of the literature on the subject it would appear that sufficient information has been contributed upon which a more or less standardized procedure might be adopted for the use of iodized oils in hysterosalpingography. In other words, it

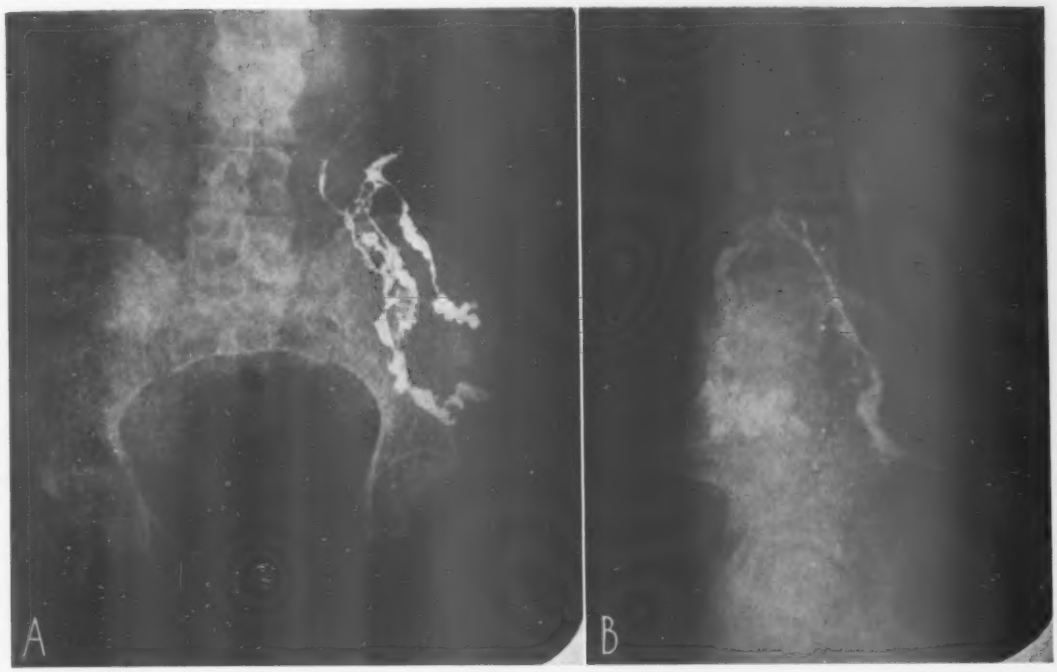


FIG. 3. Illustrating sinus tract visualization with lipiodol. *A*, this complicated sinus tract originated from a tuberculous left kidney. A large calcific deposit in kidney hilum may be seen. Anteroposterior view. *B*, lateral view of same case.

would appear that by profiting by the experience of others and by our own observations we should at this time be able to dispense with certain phases of the procedure while adhering to others and thus devise a method for hysterosalpingographies that would be comparable when done in different laboratories. It would appear that such a method should be simplified to the extent that it could be carried out in a roentgenographic department without the necessity of the patient being hospitalized and possibly without the necessity of her returning to the office for additional examination. The following procedure is suggested as meeting the above requirements for an approximately standardized method:

1. Close cooperation between the gynecologist and roentgenologist. They should work together, each carrying out his portion of the procedure as agreed upon between them. It is of greatest importance that a complete history and physical examination, including a thorough pelvic examination,

FIG. 4. Cholangiogram. This was made following subserous cholecystectomy revealing stricture of the common bile duct.

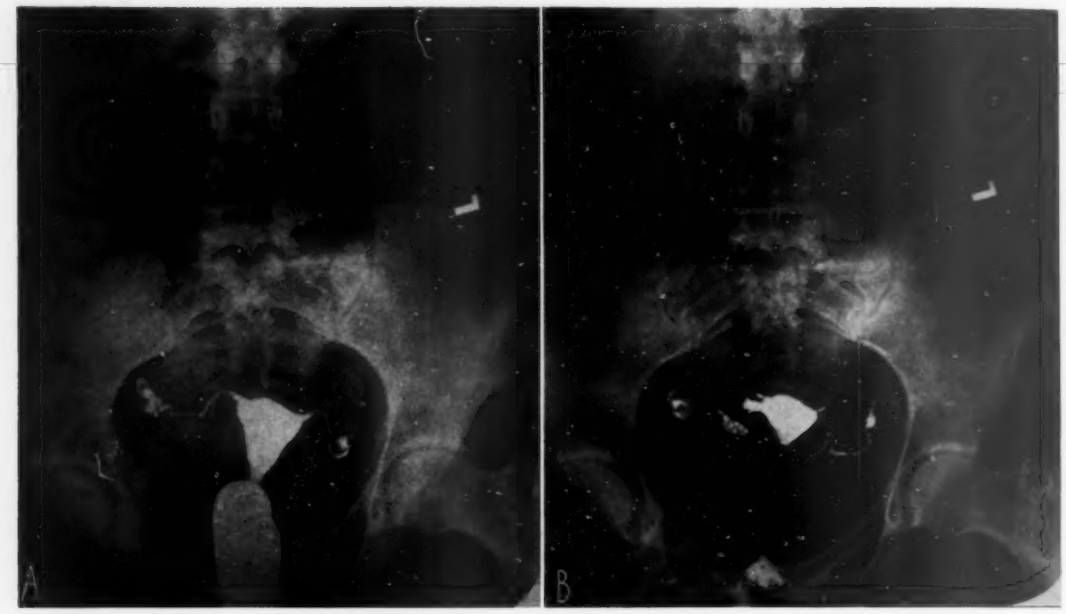


FIG. 5. Normal hysterosalpingogram. *A*, showing uterine cavity and both fallopian tubes distended with the lipiodol; *B*, fifteen minutes later following bimanual examination showing lipiodol in peritoneal cavity from both fallopian tubes.

be carried out. The pelvic examination may, of course, be done at the time of injection and should include exploration of the uterine cavity with a sound. Where the roentgenologist does not have the cooperation of a gynecologist he must conduct the above examinations himself.

FIG. 6. Showing a rather large uterine cavity with both tubes occluded.

2. The patient should receive 1/150 grain of atropine one hour prior to examination. This is reported as greatly increasing the number of tubal patencies obtainable.[10]

3. The injection should be carried out under roentgenoscopic control.[7] The patient's statements are often unreliable but it is a good indication that sufficient pressure has been obtained when the patient complains of cramp-like pains in the pelvis.

4. When sufficient oil has been injected a roentgenogram should be made. The pressure is released and instruments removed but the patient remains in the same position on the table while the film is developed and inspected. Should the roentgenogram reveal no abnormalities and if the iodized oil has penetrated into the peritoneal cavity from both fallopian tubes, no further procedure is necessary.

5. Should it appear from the first roentgenogram that one or both tubes are oc-

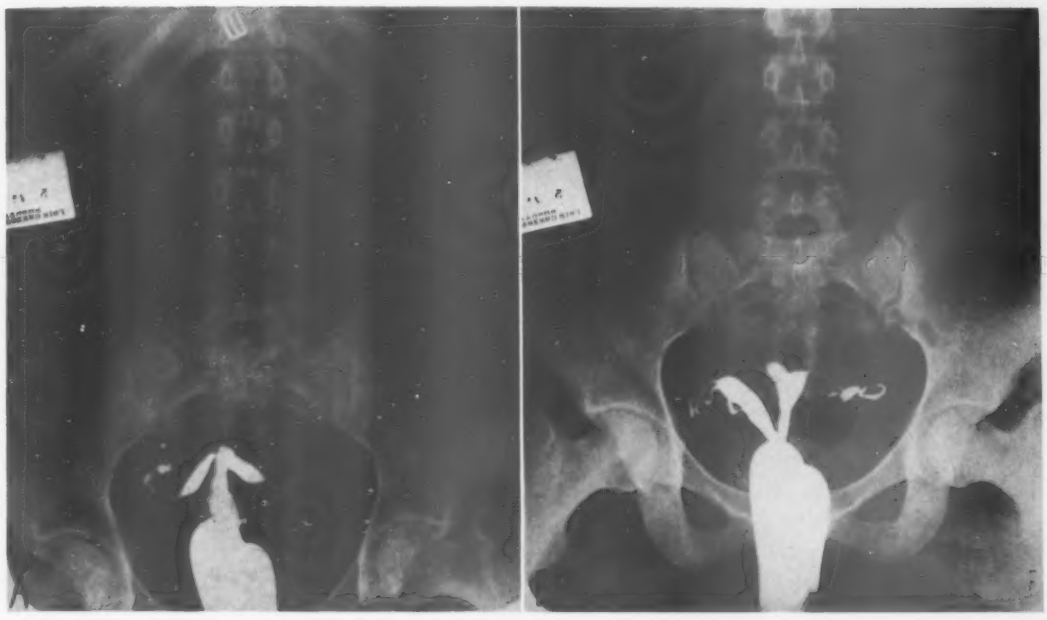


Fig. 7. Hysterosalpingogram showing double uterus. *A*, showing uterine cavity and fallopian tubes distended with the lipiodol; *B*, a few minutes later with slightly increased pressure showing that lipiodol has escaped into the peritoneal cavity.

cluded, or that they are not visualized, then a bimanual pelvic examination is made and an effort made to move the uterus and tubes about as much as possible.

6. A second roentgenogram is made. The bimanual examination will often cause some of the oil in the ends of the tubes to be extruded at once into the peritoneal cavity, or distributed about over the pelvis, the location of which may be uncertain from an inspection of the first roentgenogram. This will cause the second roentgenogram to be much more diagnostic.

In offices where roentgenoscopic control is not possible, the method of Hyams of fractional injection of the iodized oil might well be employed (see above).

From April, 1935, to January 1, 1939, a series of 180 hysterosalpingograms were made by me and following are some of the results. In 110 cases the uterus and both fallopian tubes were visualized but no lipiodol appeared in the peritoneal cavity. In 57 cases lipiodol entered the peritoneal cavity through one or both fallopian tubes (Fig. 5). In 13 cases one or both fallopian tubes failed to visualize and no lipiodol appeared in the peritoneal cavity. Only a

Fig. 8. Hysterosalpingogram showing unicornate uterus.

minor portion of these women were examined because of sterility but to investigate other pathological conditions in the pelvis. Also atropine was not used in most of them and I feel that more tubal patencies would have been demonstrated had this been done. Needless to say many interesting pathological or abnormal conditions were revealed in this series (Figs. 6, 7 and 8). Many of these conditions could not have been demonstrated by any other procedure short of laparotomy.

In 4 of the women pregnancy occurred promptly following the hysterosalpingography. All 4 delivered healthy babies. Many others could not be followed up in this respect. It is apparent that the above results do not compare well with the results of other workers but I wish to emphasize again that only a minor portion of the

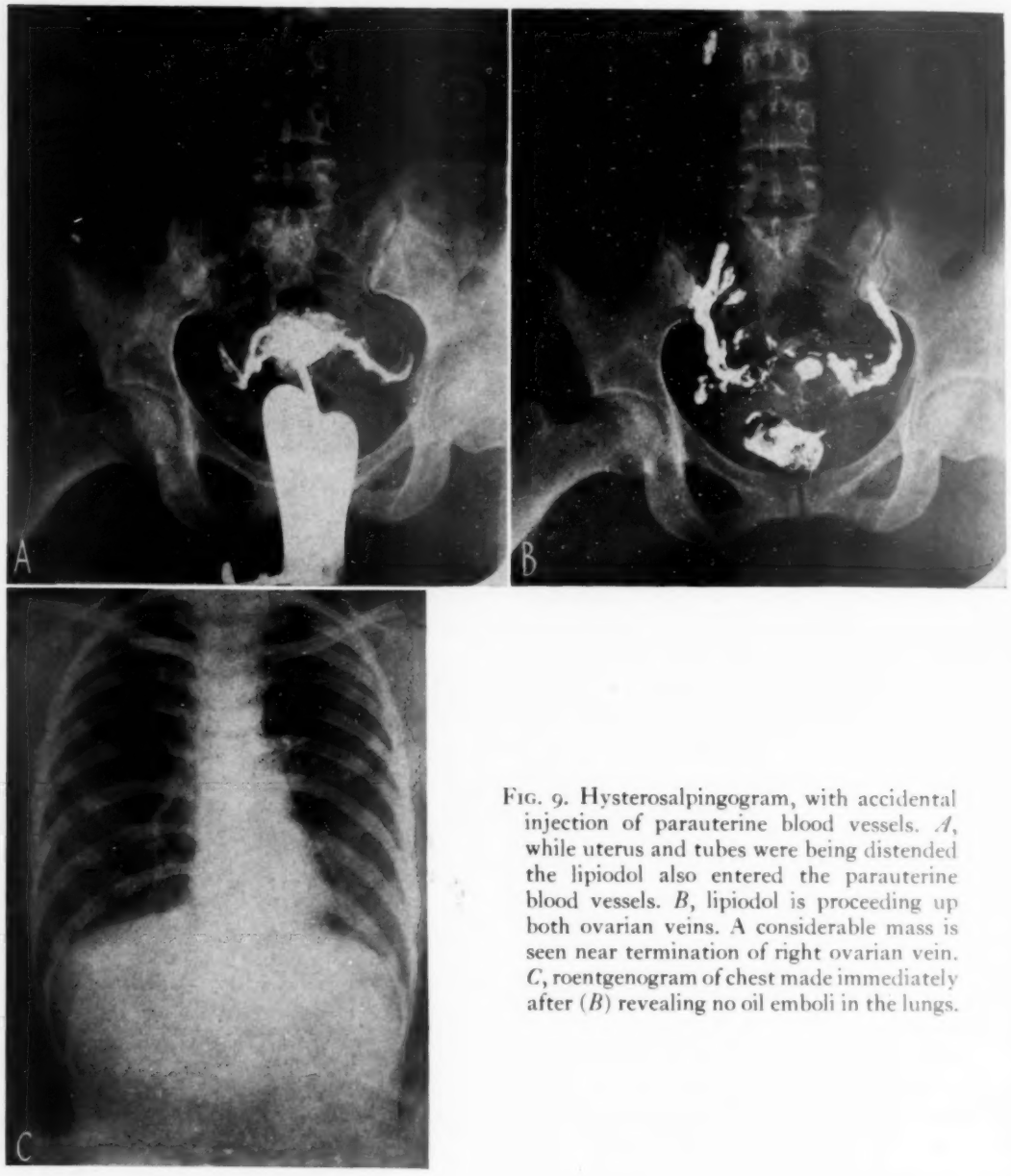


FIG. 9. Hysterosalpingogram, with accidental injection of parauterine blood vessels. *A*, while uterus and tubes were being distended the lipiodol also entered the parauterine blood vessels. *B*, lipiodol is proceeding up both ovarian veins. A considerable mass is seen near termination of right ovarian vein. *C*, roentgenogram of chest made immediately after (*B*) revealing no oil emboli in the lungs.

examinations were conducted for the purpose of investigating sterility.

It becomes necessary now to mention some untoward results that occurred in this series of cases. In 9 of the cases, more or less hysterosalpingography of sterility cases as it does in the cases where an effort is being made to demonstrate other pathological conditions. In a large series of cases one will finally be convinced that when sufficient

TABLE I

INTRAVENOUS INJECTION OF RABBITS WITH LIPIODOL

Rabbit No.	Weight	Amount Injected in Ear Vein	Roentgenogram within 5 Minutes Revealed	Roentgenogram 2 Hours Later Revealed	Period of Observation Following Injection
1. White doe, pregnant	8½ lb.	0.5 cc.	No pulmonary emboli	No pulmonary emboli	Remained healthy. Delivered 10 young ones 48 hours after injection
2. White doe	5 lb.	0.75 cc.	No pulmonary emboli	No pulmonary emboli	Remained healthy
3. White doe	7¼ lb.	1 cc.	No pulmonary emboli	No pulmonary emboli	Profuse hemorrhage from ear vein. Died in 10 days
4. White buck	7¼ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
5. White doe, pregnant	9 lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
6. White doe	8½ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
7. Red doe	7¾ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
8. White buck	6½ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
9. White buck	6¼ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
10. White doe	6¾ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
11. White doe	7½ lb.	1 cc.	Many pulmonry emboli	No pulmonary emboli	Remained healthy
12. White doe	7¼ lb.	1 cc.	Few pulmonary emboli	No pulmonary emboli	Remained healthy
13. White buck	6½ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
14. White buck	7 lb.	1 cc.	No pulmonary emboli	No pulmonary emboli	Remained healthy
15. White doe	7½ lb.	1 cc.	No pulmonary emboli	No pulmonary emboli	Remained healthy
16. White buck	8 lb.	1 cc.	Few pulmonary emboli	No pulmonary emboli	Remained healthy
17. White buck	6 lb.	1 cc.	No pulmonary emboli	No pulmonary emboli	Remained healthy
18. White buck	6½ lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
19. White doe	7 lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy
20. White buck	8 lb.	1 cc.	Many pulmonary emboli	No pulmonary emboli	Remained healthy

Above table shows that lipiodol (LaFay) can be administered intravenously to rabbits in amounts sufficient to consistently produce pulmonary emboli without causing any untoward results in animals. The one death that occurred in the animals was caused by hemorrhage from the ear vein and was not in any way due to the lipiodol itself (see also Fig. 10, *A*, *B*, *C* and *D*).

injection of the parauterine blood vessels occurred. Before some of our present safeguards were in use this injection of blood vessels was quite extensive in some cases (Fig. 9). It appears that in a certain percentage of cases in spite of all precautions there will occur an injection of the parauterine blood vessels. It appears also that this accident does not occur so often in pressure of the oil within the uterus is obtained to force the oil through normal tubes, sufficient pressure is also present to force the oil into the parauterine blood vessels should they be open or unusually permeable. Therefore, the accurate measurement of the pressure by means of manometers will not avoid this accident. In this connection it is only natural to conjecture how

FIG. 10. Sample roentgenograms of animal experimentation. *A* and *C*, showing oil emboli in lungs of rabbits. The roentgenograms were made within five minutes following injection of lipiodol in ear vein of rabbit. *B* and *D*, roentgenograms two hours later showing that oil emboli have completely disappeared. Rabbits remained healthy.

many times blood vessels are injected with air during tubal insufflation by the Rubin method. This undoubtedly does occur sometimes, although both the operator and the patient may be unaware of it.

It is believed that these accidental injections of the parauterine blood vessels are not reported in the literature as often as they should be and that it is almost certain that anyone doing a fairly large number of hysterosalpingographies will encounter this accident. I believe that all such cases should be reported and measures suggested for prevention. It is evident that roentgenoscopic control, with careful selection of cases, after complete history and physical examination, are the most important elements in the prevention of this accident.

When the first such accident occurred in my work a perusal of the literature revealed that only 38 such accidents had been reported up to that time.[12] In that series of 38 cases no untoward results occurred except in one case which died. In this one case it was indicated that the iodized oil used may have been of doubtful quality.

The first case occurring in my experience did not show any untoward results whatever, and in fact the patient was unaware that anything unusual had occurred, either then or later. Also, in the remainder of the cases in which injection of the parauterine blood vessels occurred there were no serious ill effects. All were carefully observed and followed up for months afterward. The most nearly serious ill effect that occurred was in a patient who developed a slight bronchial irritation one week following the hysterosalpingography and she reported that a slightly bloody sputum was coughed up at one time. The bronchial irritation disappeared in a few days and there was no recurrence during the next several months. Roentgenograms of the chest immediately following hysterosalpingography and also at the time of the bronchial irritation did not reveal any evidence of a pathological condition in either lung nor any evidence of oil emboli.

Roentgenograms of the chest were made in all of the cases in which injection of the parauterine blood vessels occurred and in none of them was it possible to demonstrate any oil emboli in the lungs nor any other pathological changes.

Some writers in recent years indicate that a dire calamity might be expected should this accident occur and some of their

statements indicate that a disastrous result would almost surely follow.[8,11,16] Since there was obviously a difference of opinion and since no disastrous results occurred in my own experience, I decided to carry out some animal experimentations in an effort to determine the results of intravenous injection of iodized oil.

Accordingly, 20 rabbits were injected intravenously with different amounts of lipiodol. The injections were made in the ear veins of the rabbits and enough lipiodol was injected according to body weight of the rabbit to correspond with the average amount of lipiodol used in doing a hysterosalpingography on a woman of average weight. Table 1 shows some results of this experiment.

It will be noted that none of the rabbits showed any untoward effects from the use of the lipiodol. One rabbit died of hemorrhage from the ear vein due to failure to stop the flow of blood following the injection.

It was found that oil emboli could be demonstrated in the lungs of 65 per cent of the rabbits if they were roentgenographed within five minutes from the time of the intravenous injection (Fig. 10, *A* and *C*). By making roentgenograms at frequent intervals it was found that all emboli would disappear within two hours (Fig. 10, *B* and *D*). All the rabbits ate heartily and remained healthy. Some of them were pregnant and these went on to term and delivered healthy young ones the same as other rabbits which had not been injected.

The results of this experiment are somewhat at variance with animal experiments as reported by Solal[12] who stated that he could not demonstrate any iodized oil in roentgenograms of the lungs of the animals following intravenous injection, but that the oil appeared to be immediately dispersed in the blood stream or in the capillaries of the lungs without being visualized in the roentgenograms. It will also be noted that the animal experiment is at variance with the results in patients since the patients at no time showed any evidence of emboli in the lungs. This, of course, may be explained by the fact that the animals received a larger dose intravenously according to body wight than the patients. My experience with both patients and animals, as well as the results in reported cases in the literature, lead me to believe that, while this accident should not be minimized, yet its occurrence is not frequent enough nor dangerous enough to warrant the discontinuance of this valuable procedure.[1] It also appears that the danger of this accident has been somewhat exaggerated by some writers.

SUMMARY

The use of the halogenated oils as radiopaque substances has greatly widened the field of diagnostic roentgenography. In fact, they have now become an essential part of our armamentarium.

The technique of their use has become approximately standardized in some procedures.

The technique of other procedures may also become approximately standardized and such an approximate standardization for hysterosalpingography is here proposed.

The results of animal experimentation with intravenous injection of lipiodol are reported. These results, together with my experience with 9 accidental injections of parauterine blood vessels in a series of 180 hysterosalpingographies, indicate that the danger in such an accident, when it does occur, has been exaggerated by some writers.

Injection of blood vessels may also occur while distending sinus tracts with lipiodol, indicating that roentgenoscopic control is important in this procedure.

The occasional injection of blood vessels in hysterosalpingography and in sinus tract visualization with iodized oils suggests the probability that gas is also occasionally injected into the blood vessels while carrying out the Rubin insufflation tests.

REFERENCES

1. BÉCLÈRE, C. Le passage du lipiodol dans les trompes et dans le péritoine a-t-il des inconvénients? *Bull. Soc. d'obst. et de gynéc.*, 1936, *25*, 449–457.
2. FORESTIER, J., and SICARD, J. A. *Bull. et mém. Soc. méd. d. hop. de Paris*, 1922, *46*, 463.
3. FRASER, R. H. Iodized oil (lipiodol) in otolaryngologic diagnosis. *J. Michigan M. Soc.*, 1926, *25*, 270–274.
4. GOODYEAR, H. M. Iodized oil in diagnosis of nasal sinus conditions. *Arch. Otolaryng.*, 1926, *4*, 223–227.
5. KLEITSMAN, R., and HALDRE, J. Sur la valeur thérpeutique de l'hystérosalpingographie dans le traitement de l'occlusion tubaire. *Gynéc. et obst.*, 1938, *37*, 284–294.
6. MACCREADY, P. B. Iodized oil as aid in diagnosis of chronic sinusitis and of maxillary cysts. *Boston M. & S. J.*, 1926, *195*, 464–467.
7. MORHARDT, P. E. Inconvénients et contre-indications de l'hystéro-salpingographie. *Gynéc. et obst.*, 1933, *27*, 47–58.
8. PORCHER, P. Un incident de salpingographie. *Bull. et mém. Soc. de radiol. méd. de France*, 1935, *23*, 146–150.
9. PROETZ, A. W. The Displacement Method of Sinus Diagnosis and Treatment. Annals Publishing Co., St. Louis, 1939, pp. 62–187.
10. RANDALL, L. M. Comparison of use of transuterine insufflation with carbon dioxide and roentgenograms taken after injection of iodized oil. *Radiology*, 1937, *28*, 399–405.
11. SANTE, L. R. The Chest. P. B. Hoeber, Inc., New York, pp. 16–25; 272–277; 181–183.
12. SOLAL, R. *Gynéc. et obst.*, 1935, *31*, 852–859.
13. SWEEK, W. O., HARTGRAVES, T. A., and WILLIAMS, H. G. Cholecystectomy (subserous) with cystic duct drainage and cholangiography. *Am. J. Surg.*, 1938, *40*, 552–559.
14. TITUS, P. Practical aspects of sterility studies. *Am. J. Surg.*, 1937, *35*, 345–351.
15. WAHL, F. A. Vereinfachte Technik der Salpingographie. *Zentralbl. f. Gynäk.*, 1938, *62*, 1282–1284.
16. WONG, A. I. H., WU, C., and CHIEN, M. H. Escape of lipiodol into utero-ovarian venous system in hystero-salpingography. *Chinese M. J.*, 1932, *46*, 162–167.
17. WATERS, C. A., BAYNE-JONES, S., and ROWNTREE, L. G. Roentgenography of the lungs. *Arch. Int. Med.*, 1917, *19*, 538–549.

STRAY RADIATION UNDER ACTUAL CONDITIONS*

By ROBERT B. TAFT, M.D.
CHARLESTON, SOUTH CAROLINA

UNDOUBTEDLY, every radiologist has at some time wondered whether he receives dangerous doses of radiation on his own person. The purpose of this short paper is to show that it is comparatively simple to settle the matter and make corrective steps should the laboratory in question be failing in protection.

The question as to the amount of radiation an individual may receive daily over many years and still retain health is not settled and probably never will be, but at least we can fairly safely assume that the operator who receives less than one-tenth of a roentgen per day will enjoy the same life expectancy as a member of any other profession fraught with equal nervous strain. It is highly probable that radiologists who started work many years ago when proper protective devices were not known, received much more radiation than this amount and are now in excellent health; but no one should forget that within recent years some of our most valued members have passed on as the result of blood diseases.

There are three methods of determining the amount of radiation present in various locations: the photographic film, the Geiger-Müller counter and the ionization chamber. It must be remembered that as not all of the radiation in a laboratory is of the same quality, the recording medium must be responsive to a great range. These types of radiation may be arbitrarily classed as: (1) those used in roentgenographing small parts, such as extremities; (2) those used in roentgenographing heavier parts; (3) those used in superficial therapy; (4) those used in 200 kv. therapy; (5) gamma radiation and radiation from machines in excess of 200 kv. In my opinion, a properly calibrated ionization chamber independent of wave length is the only instrument with which reasonably accurate observations can be made. The large Victoreen chamber answers this requirement, having a total scale of 0.25 r and readable to within 1/200 r, and practically independent of the above wave lengths. Numerous tests with dental roentgen films have led me to believe that they are very deceptive, as the film is much less sensitive to hard radiation than to soft. The Geiger-Müller counter has proved very valuable but not for quantitative tests. It is, however, useful in making a preliminary survey of a laboratory and thereby determining in what places tests should be made with the ionization chamber.

The following tests while accurately made in their locations cannot be accurately transferred to other laboratories, but will, however, serve as a guide by which other radiologists may judge conditions in their own laboratories.

A number of tests were made on different roentgenoscopes, those having the newer type of tube immersed in oil and metallic housings, universal tube in lead glass bowl and radiator tube in lead glass bowl. The ionization chamber placed close to such tubes failed to show any reading after long continued roentgenoscopy except in the case of the lead glass enclosed tubes when the chamber was placed in line with the cathode end of the tube where there was no lead glass protection. When the ionization chamber was worn on the chest of the radiologist outside of the lead apron, the reading was approximately 1/100 roentgen for each four complete stomach roentgenoscopies, including vertical and horizontal positions. This would certainly indicate that one doing roentgenoscopy needs an apron. It is scarcely necessary to test an apron if it is purchased from a reputable company and new enough to be in good condition. However, a test on a "light

* Read at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

weight" lead rubber apron made by placing the 25 r chamber toward the tube and the 0.25 r on the side away from the tube showed less than 1/2,000 of the amount passed through for 70 kv. radiation filtered by oil in tube plus 0.25 mm. Al and bakelite table top. It would seem that the light weight apron gives adequate protection.

Roentgenographic work offers little hazard to the technician, provided, of course, the beam of radiation is directed in some direction other than to the operator. The ionization chamber was set up outside the lead booth in a room where a moderate amount of work was being done with the newer type of oil immersed tube. The average distance from the patient to the ionization chamber was about 5 feet and after ten ordinary roentgenographic examinations, the chamber showed about 1/200 of a roentgen. In another test, six stereoscopic chest roentgenograms were made with the chamber 3 feet from the patients, and the radiation proved to be too small to influence the chamber at all. It appears from the above that in the small hospital or laboratory where only a slight amount of roentgenographic work is done, no lead screening is needed. I favor the use of a lead screen anyway, simply to teach the technician respect for roentgen radiation.

Attention is called to the fact that all of these tests were made on modern equipment and that no effort has been made to test the old style open tube bowl.

Therapy is a different matter from roentgenography as the voltages are higher and the exposures longer. While the present day oil immersed therapy tube gives very little radiation in any direction except through the portal, the secondary radiation from the body of the patient is well worth consideration. In general, the ionization chamber placed 4 feet from the body of a patient receiving 200 roentgens of 200 kv. radiation will collect about 4/100 roentgen. This will vary considerably with different sizes of portal and parts of the body but shows that neither technician nor radiologist should enter the room when the tube is in operation. Outside the therapy room with walls protected with lead according to specifications,* the intensity of radiation was too small to give an indication on the ionization chamber and caused little disturbance to the Geiger-Müller counter. The question as to whether the ceiling should be leaded can be answered only after a consideration of the conditions such as the number of treatments per day given and whether the room is occupied all of that time. My therapy room has no lead in the ceiling, the room above being used as a research laboratory and never occupied when therapy is in progress. There is scarcely radiation enough in this room to give accurate readings but, very roughly, an ionization chamber placed under a chair collects about 1/100 r for every 700 r of 200 kv. therapy. Obviously, it should not be occupied during the working day.

The handling of radium does not lend itself well to measurements but is probably the cause of greatest exposure to the operator. When radium is stored according to specifications* it is, of course, no hazard to those in the vicinity, but far too many users of small amounts of radium do not take the precaution of proper storage. For one to be bombarded throughout the course of the day by radium not even in use is foolhardy when the acquisition of a proper lead block is so simple and inexpensive. Unprotected, 75 mg. will give 1/10 r in eight hours at a distance of about 7 feet; 25 mg. will give the same amount of radiation in the same time at about 4 feet.

On account of the short distances at which radium has to be handled, the body of the operator receives much less dosage than the hands, simply by the law of inverse squares, and for the same reason ionization measurements are misleading. However, for the sake of a rough test, the chamber was tied on the chest of the radiologist while he took 75 mg. of radium

* This figure is taken from the two pamphlets, "X-Ray Protection" and "Radium Protection" obtainable from the Superintendent of Documents, Washington, D. C. It is strongly recommended that every radiologist obtain copies of these and study them carefully.

out of a safe, placed it in a cervical applicator, carried it to a nearby hospital and secured the applicator in a cervix, removed it after treatment and returned it to the safe. During this time, the chamber received 7/100 r. This at first appears alarming but it must be remembered that most of that radiation had to be received by the chamber when the radium came fairly close to it and again, by the law of inverse squares, the body of the operator did not receive anything nearly that large a dose. In addition, under actual conditions, a technician would probably prepare the radium and in that way the dose would be divided between two or more persons.

In conclusion, it appears that in a laboratory equipped with modern apparatus and staffed by careful workers, no one should receive radiation in excess of the well established tolerance dose.*

* For discussion see page 398.

PRELIMINARY STUDIES ON DOSAGE MEASUREMENTS WITH MILLION VOLT ROENTGEN RAYS

PART I.* THE MEASUREMENT OF QUANTITY AND QUALITY OF ROENTGEN RAYS IN THE SUPERVOLTAGE RANGE

PART II.† A COMPARISON OF TISSUE DOSES FROM 200 KV. AND 1,000 KV. ROENTGEN RAYS

By EDITH H. QUIMBY, Sc.D., *and* ELIZABETH F. FOCHT, B.A.
Memorial Hospital
NEW YORK, NEW YORK

PART I

WITH the continued increase in the number of supervoltage installations employed in roentgen therapy, the need for agreement as to methods of quantity and quality specification becomes important. At the present time, the term *supervoltage* is generally applied to any tube operating at 400–1,000 kv. As various installations have been completed, reports of their construction and some data regarding their radiation have been published. It should be worth while to collect the information now available from various sources, correlate it and try to arrive at some preliminary opinions regarding proper measuring methods, the value of the data already at hand, and the directions in which it is desirable to pursue further study. Accordingly, in the present paper, the authors first present results of measurements on the Memorial Hospital 1,000 kv. installation, and then attempt to correlate a considerable amount of the material found in the literature for the last few years.

A. The Measurement of Quantity. According to the recommendation of the International Units Committee, quantity of roentgen radiation should be expressed in terms of the roentgen, and quality in terms of the half-value layer in the appropriate material.[24] In the ordinary therapy range, 100–200 kv., measurements with a properly constructed free air ionization chamber meet all the requirements of the definition of the roentgen. For higher voltage roentgen rays and for gamma rays, various mechanical and physical difficulties limit the use of such chambers. Consequently, a trend has set in toward the standard employment of thimble chambers for these penetrating radiations. Nevertheless it is necessary to check the theoretically satisfactory thimble chamber measurements by independent means, and to correlate them with free air chamber measurements.

In the gamma-ray region, extensive measurements have been carried out by a number of physicists and the problem may be considered essentially solved.[15,18,26,32,47,52] In the intermediate region, of supervoltage roentgen rays, less work has been done. Some of the above-mentioned workers attempted to employ their parallel plate open air chambers in the measurement of roentgen rays in the 400–600 kv. range, but obtained rather discordant results. In general, a great difficulty appears to have been lack of sufficient spacing between the plates, but other factors have also played a part.

In view of the fact that, for gamma rays, measurements with thimble chambers have been found satisfactory, *if made under the proper conditions*, as well as for roentgen rays in the 200 kv. region, it is legitimate to assume that they will be also for supervoltage roentgen rays. However, the proper conditions for these rays have not yet been definitely set forth. Taylor and his associates[46] at the National Bureau of Standards in Washington have undertaken a comprehensive study of the problem, and

* Presented in part at the Fortieth Annual Meeting, American Roentgen Ray Society, Chicago, Ill., Sept. 19–22, 1939.
† Presented in part at the Forty-first Annual Meeting, American Roentgen Ray Society, Boston, Mass., Oct. 1–4, 1940.

have published some of their results in the 200–400 kv. range, with open air chambers and parallel plate chambers filled with air at elevated pressures.

While awaiting their correlation of such measurements with those made by means of thimble chambers, and their extension to higher voltages, one can obtain much information by the conservative employment of available chambers, of both the thimble and the extrapolation type.[14,39] With either of these instruments, an important factor is the wall thickness of the chamber. It will be remembered that many of the discrepancies in early gamma-ray measurement were due to variations in this factor. With too small a wall thickness, proper equilibrium between the primary and secondary radiation is not established. This thickness must be such that no secondary electrons arising outside the chamber can enter the measuring volume; it must, however, not be appreciably greater than this. Of course the material must be of the "air-wall" type. In the case of gamma rays, a thickness of 4 mm. of such material of unit density was found necessary and sufficient. For secondary electrons produced by million volt roentgen-ray apparatus, it would be expected to be definitely less.

For practical purposes, the necessary thickness can be determined by means of a thin-walled chamber of organic material, over which can be slipped snugly fitting shells of different thicknesses. As the total wall material is increased up to a certain point, the ionization current also increases, as electron equilibrium is established. With further increase in wall thickness, the ionization decreases, due to absorption of the primary radiation.

The proportion of secondary radiation present in a beam is in part a function of the geometry of the set-up, the relative positions of tube, filters, diaphragms, cones, etc., and the ionization chamber. If there is considerable scattering and absorbing material in the beam, the number of secondary electrons present near this material may be more than the equilibrium amount. On the other hand, after the radiation has traversed a considerable air space, particularly in the case of narrow beams, a large part of the electrons arising in the filter and other parts of the apparatus may be scattered out of the beam, while the number formed in the air is relatively small, so that there is under-compensation, or equilibrium does not exist. It is, hence, evident that the results of a study of the adequacy of any ionization chamber will depend partly on the geometry of the apparatus. (The clinical implications of this phenomenon will be discussed in Part II.)

In June, 1939, a one million volt roentgen-ray machine was installed at the Memorial Hospital. This apparatus has been described in detail elsewhere.[5] It is only necessary to state here that the target is of the transmission type, set at an angle of 45° to the cathode-ray stream. The roentgen-ray beam can be utilized at any angle within a range from the direction of the cathode-ray stream to a perpendicular to this direction. The inherent filtration is high, approximately 2 mm. tungsten, 8 mm. copper, 2 mm. mercury, and several millimeters of water.

As the first step in the study of the radiation from this tube, the effect of wall thickness of the chamber was investigated. Preliminary measurements were made with a small thimble with shells as described above. This was placed in a small beam, at a distance of about 70 cm. from the tube holder or any other scattering material, and it was found that readings increased with successive shells until the total wall thickness was just over 1 mm. of organic material (celluloid, of slightly more than unit density).

For a more detailed study of this subject, an ionization chamber of the extrapolation type was employed. The experimental arrangements are shown in diagram in Figure 1. The tube is surrounded by a mercury shutter, through which a movable channel permits the passage of the beam of radiation in any desired direction within the limits specified above. Geared to this chan-

nel, in such a way that it always acts as a diaphragm, is the 2½ inch thick lead shield (fixed diaphragm of Fig. 1), having an opening 8.5×8.5 cm., at a distance of 23 cm. from the focal spot. Below this can be inserted various removable lead diaphragms 1 inch thick and with a wide range of apertures. At a distance of 79 cm. from the target, and 45 cm. from the limiting diaphragm, the extrapolation chamber was

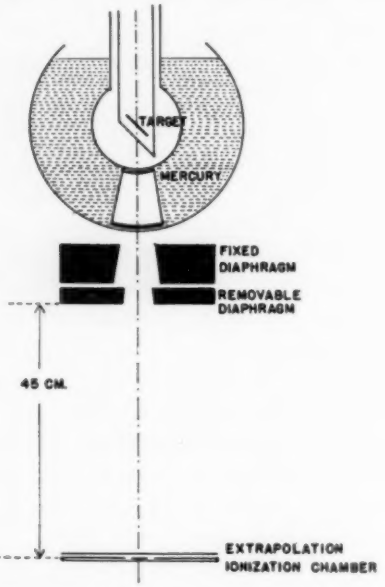


FIG. 1. Diagram showing relative positions of target of 1,000 kv. roentgen tube, diaphragms, and ionization chamber.

supported on a large cardboard carton, with a hole in the top considerably greater than the diameter of the largest roentgen-ray beam used in this study, so that there was no scattering material in the beam for a distance of more than 50 cm. below the chamber.

The lower electrode of the chamber consists of two sheets of lucite, each 1.5 mm. thick, fused together under pressure, with a fine steel wire between them, extending diagonally across the sheets.* A very small hole bored from the center of one surface to the steel wire, and filled with graphite, provides an electrical connection. The entire surface of the plate, 30 cm. in diameter, is coated with aquadag to provide electrical conductivity. At its center, a circle 3 cm. in diameter is scribed with a sharp compass, removing the aquadag and forming an insulating barrier between the areas inside and outside it. The area inside forms the collecting electrode, connected through the central steel wire to the cable leading to the measuring instrument, the area outside is grounded to form a guard ring, since the collecting electrode is practically at ground potential during measurement. The upper electrode, carried on micrometer screws for adjusting the spacing between it and the lower one, can be of any desired material. By determining the electrical capacity of the ionization chamber as a parallel plate condenser, the spacing between the electrodes, and hence the volume of the chamber, can be accurately calculated. The measuring instrument is of the Failla vacuum tube type.[12]

The experimental procedure was as follows: An upper electrode of thin silk chiffon, stretched tightly on an aluminum frame and coated with India ink to provide electrical conductivity, was employed for the first series of measurements. With this in place, and an arbitrary setting on the micrometers, a measurement was made of the electrical capacity as mentioned above, and the spacing thus determined. The roentgen rays were then turned on, and the ionization current measured in arbitrary units. For several larger and smaller micrometer settings, similar measurements were made. The range was thus determined within which the ionization per unit volume was constant and all measurements were conducted within this range. A sheet of ash free filter paper was then laid on the electrode, the ionization measured, and the spacing again determined; this was repeated for a number of sheets of paper. As these were laid on the chiffon electrode, it was, of course, depressed, so that the spacing became less, but the ionization *per unit volume* increased steadily. After 10 sheets of paper had thus been piled up, it

* These fused sheets with the included wire were prepared by the DuPont Company. It is a pleasure here to acknowledge their kind cooperation.

was deemed advisable to exchange the chiffon electrode for one of thin parchment and repeat the procedure with this until a point was reached after which there was no more increase in ionization. The data thus obtained, for a 100 sq. cm. beam at the ionization chamber, are given in Table 1, and shown graphically in Figure 2. For larger beams the increase was not so great, for smaller beams it was greater, but the maximum occurred for essentially the same thickness in each field. The analysis for the large and small beams was not as complete as for the one at 100 sq. cm.

Table I

EFFECT OF WALL THICKNESS ON IONIZATION: EXTRAPOLATION IONIZATION CHAMBER 1,000 KV., HIGH INHERENT FILTRATION, 100 SQ. CM. IRRADIATED AREA, AREA OF COLLECTING ELECTRODE 6.92 SQ. CM. FOCAL-CHAMBER DISTANCE 79 CM. ROENTGEN RAYS IN DIRECTION OF CATHODE STREAM

Material of Upper Electrode	Weight of Upper Electrode mg./sq. cm.	Spacing between Electrodes cm.	Chamber Volume cc.	Ionization Arbitrary Units	Ionization per cc.	Per Cent
Chiffon	1.29	2.61	1.81	4.15	2.29	100
+ 1 paper	6.35	2.42	1.67	4.50	2.69	118
+ 2 paper	11.41	2.18	1.51	4.65	3.08	135
+ 3 paper	16.47	1.95	1.35	4.63	3.43	150
+ 4 paper	21.53	1.80	1.25	4.55	3.64	159
+ 7 paper	36.71	1.34	0.93	3.73	4.00	175
+10 paper	51.89	1.03	0.71	2.94	4.14	181
Parchment	18.0	2.77	1.92	6.20	3.23	141
+ 1 paper	23.06	2.74	1.90	6.63	3.49	153
+ 3 paper	33.18	2.74	1.90	7.08	3.74	164
+ 5 paper	43.30	2.77	1.92	7.65	4.00	175
+ 7 paper	53.42	2.78	1.92	7.85	4.09	179
+10 paper	68.60	2.77	1.92	8.10	4.23	185
+15 paper	93.9	2.78	1.92	8.50	4.43	194
+20 paper	119.2	2.74	1.90	8.61	4.54	198
+25 paper	144.5	2.74	1.90	8.50	4.48	196

From these data it is apparent that a wall thickness of over a millimeter of unit density material is necessary for the establishment of electron equilibrium with roentgen rays generated at 1,000 kv., with an open port and a diaphragm to chamber distance of about 45 cm. Actually, allowing for the absorption of the primary roentgen rays in the chamber wall, the correct value is about 1.5 mm. Other distances were not investigated, since it was proposed to employ essentially the same geometry in therapy, the patient taking the place of the ionization chamber. All data presented in Part I of this paper, unless otherwise specified, were obtained with a thimble type chamber having a wall thickness of about 1.5 mm. of organic material. For the material presented in Part II, either this same thimble chamber, or the extrapolation chamber with a sufficiently thick upper electrode, was employed, as specified in the various sets of data. Unless otherwise stated, all measurements were made at about 70 cm. target-chamber or target-skin distance.

The measuring instrument has been calibrated to determine ionization current in electrostatic units per second. If the volume of the ionization chamber is known, the intensity of the roentgen-ray beam can be determined in terms of roentgens per minute, *provided the ionization chamber is suitable for the measurement of the roentgen rays in question*. Within practical limits, it may be assumed that the chambers herein specified are thus suitable, and doses discussed

in the second part of this paper will be specified in roentgens. It must be remembered that one roentgen of 1,000 kv. roentgen rays does not represent the same total energy, or the same ion distribution as one roentgen of 200 kv. radiation, but simply the same number of ion pairs produced in the ionization chamber under conditions fulfilling the

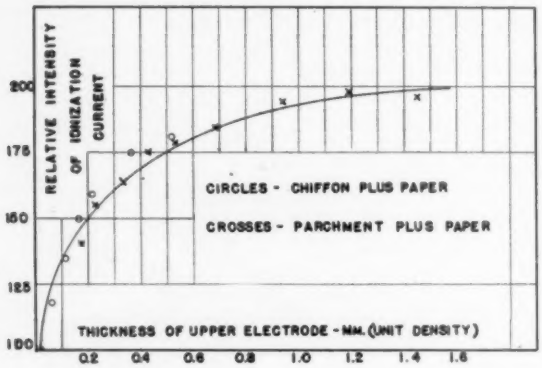


FIG. 2. Curve showing increase in ionization with increase in thickness of upper electrode of extrapolation ionization chamber; 1,000 kv. roentgen rays, half-value layer 3.8 mm. Pb.

requirements of the definition of the roentgen. Equal numbers of roentgens of the two kinds of radiation need not be expected to produce the same biological or clinical results; this is a matter which requires an entirely separate investigation.

The determination of the roentgens per minute in the beam in air, made with the extrapolation chamber, a small spherical air-wall chamber used at the Memorial Hospital as a secondary standard, and 25 r and 100 r Victoreen chambers all agreed within 2 per cent.* Accordingly it appears that measurements of quantity of radiation in air made with chambers of any of these types, or with other small, sufficiently thick air-wall chambers, should all be comparable.†

B. The Measurement of Quality. The specification of roentgen-ray quality is to be made, according to the recommendations of the International Units Committee, in terms of the half-value layer in a suitable substance.[24] Copper is recommended for the region from 120–400 kv., and tin is suggested for higher voltages. As each new supervoltage installation has been put into use, a certain amount of absorption data has been published, from which inferences can be made as to the quality of the radiation. However, in general each installation has been studied from a particular point of view, often for a single beam of radiation, and by means of measuring instruments whose characteristics at these voltages are not well known. Little attempt has been made either to develop a standard technique or to make measurements in such a manner that they can be compared with those obtained in other institutions. In many cases it has not been possible to determine the voltage directly with any degree of accuracy. The inherent filter in various tubes differs greatly, and a basis for comparison in such a case has not been developed. Further, both the quality and the intensity of the beam of radiation from any tube in the neighborhood of 1,000 kv. depends

* For the use of the Victoreen instrument, we are indebted to Dr. Carty and Dr. Tuggle, of the Department of Radiology of New York Hospital.

† A consideration that must not be overlooked in connection with the measurement of quantity of radiation is the applicability of the method to determining tissue dosage in therapy. Biological effects result from ionization in the tissues. It is not possible, as yet, to measure this, and tissue dosage is conventionally expressed in terms of the ionization produced in air in an "air-wall" chamber within the tissues, or within a phantom. This assumes that a constant ratio exists between roentgen-ray ionization in air and in the tissues. If such a constant relation does not exist, then the determination of tissue doses by this method is subject to errors whose magnitude depends on the variations in the ratio.

Although it is not possible directly to measure the ionization in tissue, Failla suggested that it should be possible to prepare a gas mixture of the elements occurring in the body, in the same proportions, and to compare the ionization in this with that in air. This was done by Naidu[25a] for a range of voltages from 25 to 200. He found the ratio of ionization in the gas mixture to that in air to increase 22 per cent within this voltage range, and his data indicate that it will continue to increase with higher voltages, at least for a time. The inference to be drawn from this is that, for equal tissue doses measured with the air-wall chamber, the tissue is more strongly ionized at the higher voltages. Such measurements have not yet been made above 200 kv. It is not to be expected that the ratio will continue to increase at the same rate into the 1,000 kv. region, since the variation is due mainly to changes in the photoelectric absorption, which becomes negligible at such voltages. However, it must be remembered that the radiation in the depths of the body is considerably softer than the primary beam, and that this softer radiation, which is actually producing the tissue ionization, may be within the range in which variation in the ratio is significant.

In view of these considerations, it is apparent that there is definite need for further study of quality changes of radiation within the body, and of the effect of these changes on tissue dose,

greatly on the angle between the roentgen-ray beam and the cathode stream.[7]

Since standard methods for determining quality in this region may not be established for some time, it appears desirable to see what correlation can be made among existing data, and to investigate the possibilities of comparing qualities and doses in the 400–1,000 kv. region.

Few papers have been published covering any significant part of this range, although there are a number containing data for a single voltage. An exception to this is the work of Folsom.[17] He gives sets of absorption curves in lead and in copper for a range of voltage from 350 to 650 constant potential; his tube having an inherent filtration of approximately 2.5 mm. copper. The roentgen-ray beam used was at right angles to the cathode-ray stream; ionization measurements were made by means of a large parallel plate open air chamber. Variations of this chamber from an actual standard chamber, or from a suitably thick-walled thimble chamber are not known. The voltage was measured directly by means of a spark gap provided with 50 cm. spheres.

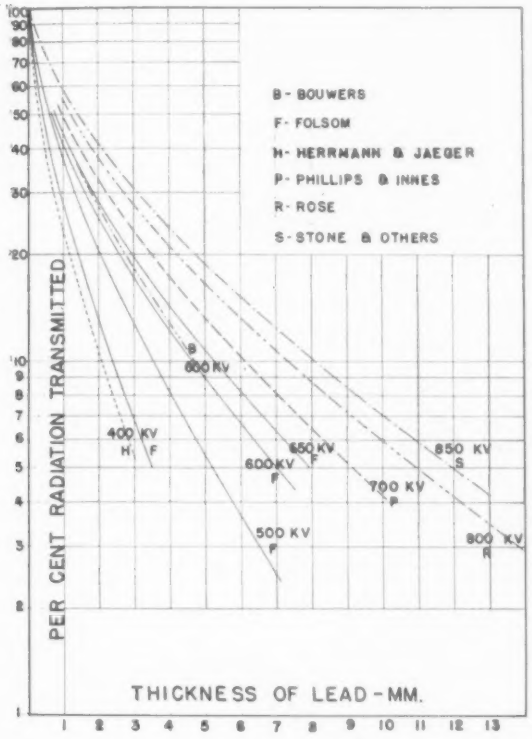


Fig. 3. Absorption curves in lead for 400 to 850 kv. roentgen rays; beam at 90° to cathode stream; total filtration approximately 3 mm. Cu. (Collected from the literature.)

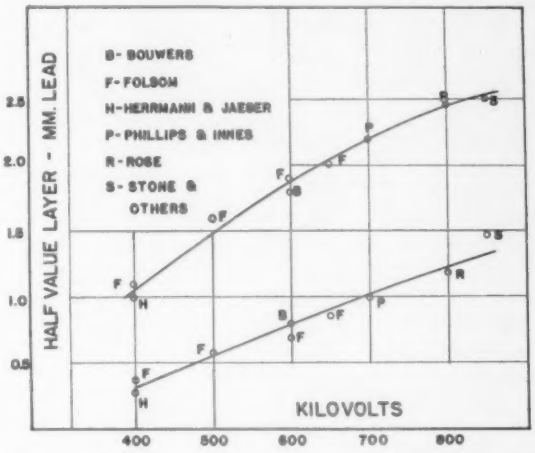


Fig. 4. Lead half-value layers from Figure 3. *Lower curve*, half-value layer of radiation with reported filter. *Upper curve*, half-value layer with 2 mm. Pb additional filter.

Folsom's curves for lead are shown in Figure 3, together with others made with thimble chambers for radiation in this voltage range, with either constant potential or high filament bias, with the same angle (90°) between the cathode-ray stream and the roentgen-ray beam, and with low inherent filtration (2 to 3 mm. copper). It would have been desirable to correct these curves to the same initial filtration. This does not appear practicable, since in most cases the tube construction was of steel, for which absorption curves are not given. Instead, the approximate inherent filtration has been listed for each source, in Table II, together with the methods of determining the voltages. References to the original publications will be found in the list at the end of this paper.[2,17,22,23,33,42,45,49] Similar, but less extensive, sets of data can be collected for copper and tin absorptions. Since the filtrations employed are not very different and the curves group themselves

TABLE II

FILTRATION AND METHOD OF VOLTAGE MEASUREMENT FOR DATA OF FIGURE 3 AND FIGURE 5

Authors	Filter	Voltage Determination
Bouwers and van der Tuuk	Unstated inherent filter + 2.5 mm. Cu +1 mm. Al	Current through an induction-free parallel carbon resistance. Also, 50 cm. sphere gap
Folsom	3 mm. steel, 3 mm. Al About 10 mm. water	50 cm. sphere gap
Hermann and Jaeger	Unstated inherent filter + 1 mm. Cu +1 mm. Al	50 cm. sphere gap
Phillips and Innes	3.2 mm. steel + 1.5 mm. Al	50 cm. sphere gap. Also oil-immersed resistance voltmeter
Rose	3.0 mm. brass +2 mm. Al +about 10 mm. water	Electrostatic voltmeter
Stone, Livingstone, Sloan and Chaffee	3 mm. steel +3.5 mm. Cu	Comparison of absorption curves with those obtained in other institutions
Hudson	[illegible] mm. Cu +2 mm. Al	Current through high resistance in parallel with tube
Van Atta and Northrup	1.5 mm. Pb +3 mm. Cu	Generating voltmeter
Memorial Hospital	2 mm. tungsten +8 mm. Cu +2 mm. Hg +10 mm. water	Linear extrapolation from low voltage calibration on basis of known relation between secondary voltage and charging current

well according to voltage, it appears that all the measurements have been made by sufficiently similar methods for comparison in the present discussion.

An idea of the relation of kilovoltage to half-value in lead can be obtained from this set of curves; lead half-value layers determined thus are shown in the lower curve of Figure 4. In spite of variations in tube construction (inherent filter) and method of measurement, these values lie on a fairly smooth curve with voltage. In practice, considerably more filter than that inherent in the tube is always employed in this voltage range; the upper curve of Figure 4 shows the half-value layers in lead for all these beams with an additional filter of 2 mm. of lead. The data available are not sufficient for the construction of similar curves for copper or tin half-value layers.

It is, of course, possible to obtain the same half-value layers at different voltages, by the employment of different filters. In Table III are indicated the lead filters (in addition to the inherent filter) necessary to obtain a half-value layer of 2 mm. of lead with each of these voltages.

TABLE III

KILOVOLTAGE AND LEAD FILTER NECESSARY TO OBTAIN HALF-VALUE LAYER OF 2 MM. LEAD. INHERENT FILTRATION APPROXIMATELY 3 MM. CU. BEAM AT RIGHT ANGLES TO CATHODE STREAM. CONSTANT POTENTIAL OR HIGH BIAS

Voltage kv.	Additional Lead Filter mm.
600	2.5
650	2.0
700	1.5
800	1.0
850	0.8

Since the outputs of the different tubes vary greatly, it is not possible to express directly the relative intensities per milliampere for these beams of the same half-value layer.

Unfortunately, this set of curves cannot be carried to higher voltages. The only available data at 1,000 kv. for radiation perpendicular to the cathode stream appears to be that obtained at the Memorial Hospital, and in this case the inherent filtration is very much greater than for the beams under discussion.

In the region of a million volts or higher, for roentgen rays in the direction of the cathode stream, in addition to the measurements made at the Memorial Hospital, are those published by Hudson[23] for 1,000 kv. constant potential, and by Van Atta and Northrup[19] for 1.0, 1.5, and 2.0 million volts. Their lead absorption curves are collected in Figure 5, together with one ob-

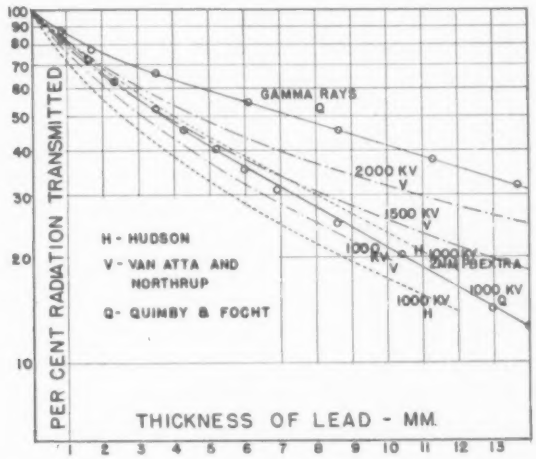


Fig. 5. Absorption curves in lead for 1,000 to 2,000 kv. roentgen rays, and gamma rays; roentgen rays in the direction of the cathode stream; high inherent filtration (*solid curves*, authors' experiments; *broken curves*, from the literature).

tained at the Memorial Hospital for gamma rays. The measurements of Van Atta, Northrup, and Hudson were made with a Victoreen instrument whose wall effect had not been investigated at these voltages. In view of the data presented earlier in this paper, this chamber may be considered suitable at one million volts, but must be questioned for higher voltages. Hudson's inherent filtration is approximately 5 mm. copper, that of Van Atta and Northrup, approximately 1.5 mm. lead and 3 mm. copper; that at the Memorial Hospital is approximately 2 mm. tungsten, 8 mm. copper, and 2 mm. mer-

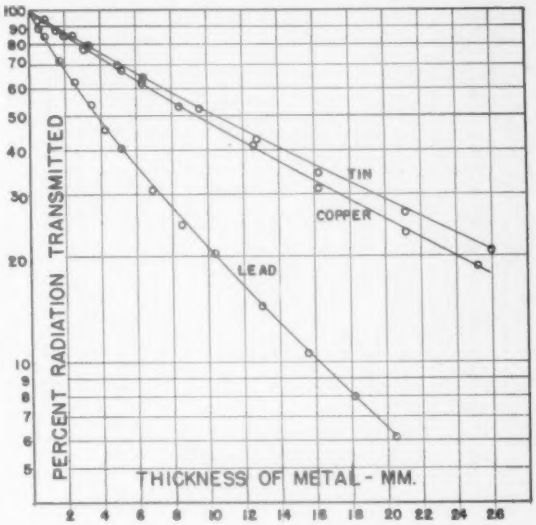


Fig. 6. Absorption curves in tin, copper, and lead, for 1,000 kv. roentgen rays; beam in direction of cathode stream; high inherent filtration.

cury. The lead half-value layers can be read directly from the curves.

A study of the absorption of million volt roentgen rays in other materials than lead is of interest. In particular, the absorption in tin and in copper should be investigated, with regard to their suitability as half-value layer standards. It was mentioned above that the International Units Committee had recommended the use of copper up to 400 kv. and of tin beyond that, but no real study of the two had been made. In Figure 6 are given absorption curves for lead, copper, and tin, for the beam of million volt roentgen rays in the direction of the cathode stream. It is somewhat surprising to note that at this voltage the absorption by copper is greater than that by tin; in other words, the half-value layer in tin is greater than in copper. This difference has not previously been brought out, although on the

curves of Phillips and Innes a greater half-value layer in tin is shown than in copper, for 700 kv. and more than 2 mm. of lead filter. Hudson's data do not show this difference, although they do indicate a possible coming together of copper and tin half-value layers at a million volts and something more than 6 mm. lead filter. This point warrants further study. Certainly

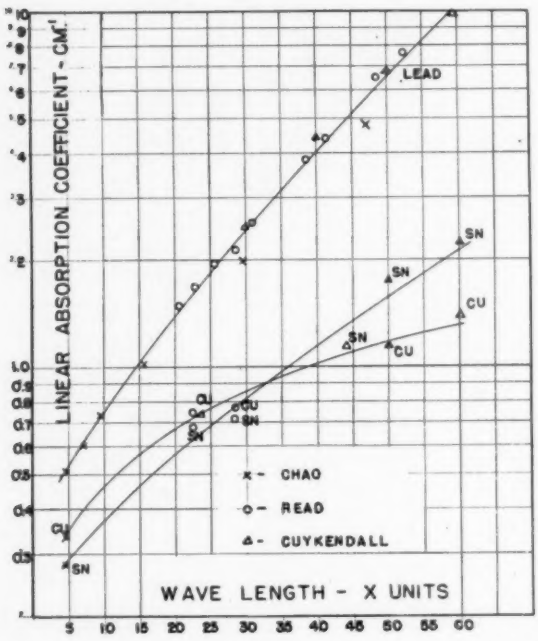


FIG. 7. Monochromatic linear absorption coefficients for lead, tin, and copper, from 5 to 60 X.U. (Collected from the literature.)

there is no advantage in going from copper to tin as a material for measuring half-value layers under these circumstances.

It is desirable to ascertain whether there is a crossing over of tin and copper absorption coefficients with monochromatic radiation. Unfortunately there are few experimental data available in the region below 50 units. However that of Cuykendall,[8] Jones,[25] Read,[40] and Chao[4] appear to settle the point. In Figure 7 are plotted linear absorption coefficients for lead, tin, and copper, based on values as indicated. Although the points are somewhat scattered, there is no doubt that the absorption coefficients for tin and copper are equal at about 30 x units (about 400 kv. monochromatic equivalent, or in the neighborhood of 800 kv. pulsating potential), and for shorter wave lengths the coefficient for copper is the higher. It is therefore of no advantage to shift from copper to tin in half-value layer specifications. Probably either the shift should be made from copper to lead at about 700 kv., or copper should be employed throughout the range to and above 1,000 kv. This matter cannot be settled at the present time.

Other possibilities for the expression of quality in the supervoltage region are the specification of absorption coefficient in lead, the equivalent wave length or the equivalent monochromatic voltage, based on such a curve as the upper one in Figure 7, the absorption coefficient being obtained in the usual manner. This method has had various advocates, among them Corrigan[6] and Lauritsen.[27] It is, of course, open to the same objections in this voltage range as at lower voltages. However in the 200–400 kv. region, tubes and apparatus are now fairly well standardized and the copper half-value layer specification has been adopted as a simple and convenient method. In the higher voltage region under consideration at present, there is no standard as yet, and one criterion for quality specification must be that it shall convey an idea of the radiation under discussion, in relation to other beams. It remains to be determined how this can best be done.

One other suggestion, at least, deserves consideration, namely the possibility of two sorts of quality specification, one, from a physical point of view, either the half-value layer in a heavy metal, or one of the factors specified in the preceding paragraph; the other, from a biological or clinical point of view, the half-value layer in water or some other organic material. Lauritsen[27] has recommended the determination of the half-value layer in water as a means for determining the equivalent voltage or wave length in terms of monochromatic radiation. He has published a curve to be employed for this purpose. Since, however,

this curve is calculated, and not based on any experimental data, its use is not recommended without further investigation. The half-value layer of the 1,000 kv. radiation employed at the Memorial Hospital is 10.3 cm. pressdwood.

The variation in quality and intensity of the beam at various angles to the cathode stream has been mentioned above. This problem was analyzed by Corrigan and Cassen,[7] on a basis of experimental data obtained in the region of 500 kv. The variation in intensity with angle for the Memorial Hospital installation is shown in Figure 8. Since the target is set at an angle of 45° to the cathode stream, the filtration at 0 and at 90° is the same, that at 45° only 0.7 times as much. Hence the direction of the true maximum cannot be determined from this curve, but it is evidently close to the direction of the cathode stream. The half-value layer of the beam in the direction of the cathode stream is 3.8 mm. of lead, in contrast to 3.1 mm. of lead for the beam at right angles to this.

PART II

Dosage in roentgen therapy is expressed in terms of the number of roentgens delivered at the point in question—in air, on the skin, or in the tumor. It may also be expressed as a percentage of an erythema dose, or in terms of other clinical or biological units. In the last analysis, all of these methods depend on some form of ionization measurement. Either the intensity of the beam is measured in air, and skin and depth doses calculated from phantom measurements, or the dose is measured on the skin, and the depth dose calculated, except in the rare instances when it is possible to introduce an ionization chamber at the site of the lesion. Even when the so-called biological units are employed, they are themselves determined or checked by ionization measurements.

The question of air and phantom measurements in the 200 kv. region has been thoroughly studied by a number of physicists, and the present status of the matter set forth in detail in Technical Bulletin No. 1 of the Standardization Committee of the Radiological Society of North America.[37] For supervoltage radiation, an ionization chamber known (or assumed) to be satisfactory at 200 kv. has ordinarily been employed. As stated in Part 1 of this paper, there appears to have been little study of the characteristics of chambers at higher

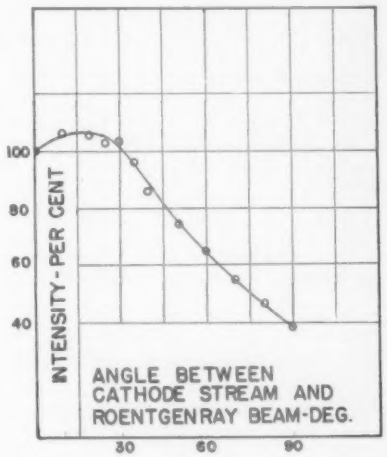


Fig. 8. Curve showing variation in intensity of 1,000 kv. roentgen-ray beam with variation in angle between cathode stream and roentgen-ray beam. Target at 45° to cathode stream; transmitted beam; inherent filtration approximately 2 mm. tungsten, 8 mm. copper, 2 mm. mercury, 10 mm. water.

voltages. The significance of the wall thickness was there brought out; the shape and volume may also be significant. The employment of the extrapolation type of chamber has been discussed in detail in previous publications.[14,39]

For the study of surface and depth doses with the 1,000 kv. roentgen-ray machine at the Memorial Hospital, the same extrapolation chamber was employed as in the work discussed in Part 1 of this paper, with the pressdwood phantom which has been used at the Memorial Hospital for all such measurements for several years. All measurements, unless otherwise specified, were made with sufficiently thick electrodes to insure electron equilibrium in the chamber. It was found that for electrode separations

from 0.5 to 4.0 mm. the ionization per unit volume was constant, both on the surface and in the depths of the phantom, and all measurements were made within this range. For every setting, the spacing, and hence the volume of the chamber, were determined as described in Part. 1.

Skin Dose. The backscatter was determined directly for a 100 sq. cm. field (10×10 cm. square), by making measurements with the extrapolation chamber in air and on the phantom in immediate succession. It was found to be, for this field, 10 per cent of the air dose, so that the skin dose is 110 per cent of the air dose. For other fields, the method employed was to determine the variation in air dose with size of beam, and the variation in skin dose with irradiated area. From this information, together with the accurate measurements of air and skin doses for the 100 sq. cm. field, the backscatter for any field can be determined. Values for this are shown in Figure 9.

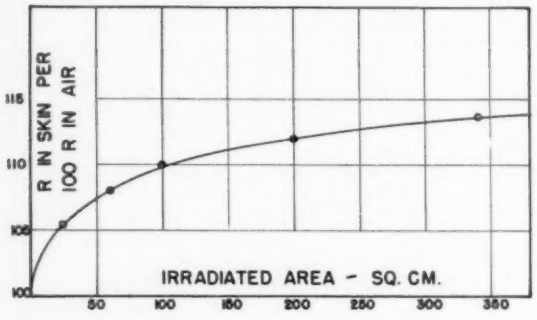


FIG. 9. Curve showing skin doses for 1,000 kv. roentgen rays per 100 r measured in air; various fields.

The backscatter for the 100 sq. cm. field was also determined with the Memorial Hospital thimble chamber and with the Victoreen chamber mentioned in Part 1. It was there stated that the three agreed in air measurement to within ±2 per cent. The same agreement was found on the surface of the pressdwood phantom. Reports of backscatter values in the supervoltage range include the following, all of which are in good agreement with the above:

Phillips and Innes,[32] 100 sq. cm., 750 kv., 10 per cent.
Van der Tuuk,[50] 100 sq. cm., 800 kv., 9 per cent.
Stone and Aebersold,[41] 400 sq. cm., 1,000 kv., 14 per cent.
Trump and Cloud,[48] 1,000 sq. cm., 1,200 kv., 7 per cent.

Depth Doses. Since the million volt machine has been available to the physics department only a few hours each day, it was desirable to develop a method for studying depth doses in steps and without the necessity of numerous check readings. Accordingly they were determined in the following manner: Using the extrapolation chamber, the depth dose curve for a 10×10 cm. field was measured very carefully, all the work being done in a single long run, and the surface dose being checked before and after the dose for each depth. Then, for a considerable number of convenient depths, at approximately 2 or 3 cm. stages, the variation in ionization with field was determined. Since the actual doses at all depths, for one field, had been measured as stated above, those for the other fields employed could be determined at each depth by calculation from the relative ionizations. By this method, depth dose curves were obtained for all the fields employed in therapy with this machine. As an additional check, several points on the depth dose curves for a 20 sq. cm. field and a 330 sq. cm. field were determined directly. In all cases the agreement was excellent. The percentage depth doses for a wide range of fields and a 70 cm. focal-skin distance are given in Table IV.

The literature contains few complete depth dose curves or isodose charts for supervoltage radiation. Most of the investigations appear to have been confined to a study of the depth dose at 10 cm. These will be considered later. Phillips and Innes[33] have published an isodose chart for 700 kv., for a 100 sq. cm. field and a 60 cm. focal-skin distance. They used a wax phantom, so that their doses would be expected to be slightly high. Stone and Aebersold,[41] and Aebersold and Chaffee[1] have published a number of depth dose curves for 1,000 kv., half-value layer 7.0 mm. pressdwood, at 80 cm. distance, using rice and pressdwood

phantoms respectively, and a Victoreen measuring instrument. When allowance is made for the difference in distance between their measurements and those of Table IV, their doses are all slightly lower, as would be expected from the difference in half-value layers in pressdwood. Their values at 200 kv., determined by the same method, are in satisfactory agreement with those determined at the Memorial Hospital for the same quality of radiation. It appears, therefore, that this difference in supervoltage depth dose is a true one, due to a difference in the quality of the radiation. Further data on variations in depth dose with voltage, for special cases, will be given below.

TABLE IV

PERCENTAGE DEPTH DOSES—1,000 KV.

Half-value Layer 3.8 mm. Pb or 10.3 cm. Pressdwood, 70 cm. Focal-Skin Distance

Depth cm.	Irradiated Area—Square Centimeters					
	20	50	100	200	300	400
	Percentage Depth Dose					
0	100	100	100	100	100	100
2	91	95	98	99	100	100
5	68	72	76	78	79	80
7	55	59	63	66	67	68
10	41	44	48	51	53	54
12	34	37	41	44	45	46
15	25	28	31	33	35	36
20	16	18	20	22	23	24
25	10	12	13	14	15	16

The difference between depth doses obtained with an extrapolation chamber and a thimble chamber has been shown to be appreciable in the 200 kv. region.[38] Accordingly it seemed desirable to make a comparison at 1,000 kv. Using the same phantom, and all other conditions the same as for the extrapolation chamber measurements, the depth dose curve for the 10×10 cm. field was determined by means of the small spherical chamber (1.54 cc. volume) which has been mentioned in Part I of this paper. This curve and the one obtained by means of the extrapolation chamber are shown in Figure 10. Results obtained with the thimble type chamber are 2–5 per cent higher than those with the extrapolation chamber. Reasons for this are not obvious, but are probably concerned with the difference in the thickness of the ionized volume in the two cases. The problem deserves further investigation. (It was not practicable to study depth doses with the Victoreen instrument.)

Exit Dose. The exit dose, the portion of the radiation traversing the body and emerging on the opposite side, is, of course, more likely to be important at 1,000 kv.

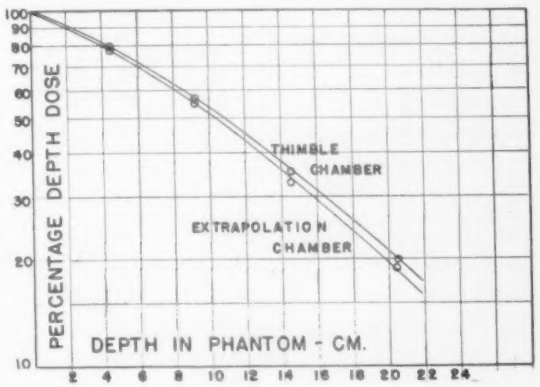


FIG. 10. Curves showing percentage depth doses for 1,000 kv. roentgen rays; half-value layer 3.8 mm. lead; 100 sq. cm. field, 70 cm. focal-skin distance. *Upper curve*, thimble chamber; *lower curve*, extrapolation chamber.

than at 200 kv. The exit dose for a given body thickness is less than the dose measured at the corresponding level in a large phantom, by the amount contributed at that level by scatter from material deeper in the phantom. If, however, the surface of the body rests on a mattress and table which may scatter the radiation back, this difference is partly or entirely compensated for. For 200 kv. radiation, the exit dose is of the order of 25 per cent less than the corresponding dose in the full phantom, and the difference may be significant.[35] At 1,000 kv. the backscatter is much less than at 200 kv. and the difference between the exit dose and full phantom dose correspondingly less; actually the exit dose is of the order of 10 per cent less than the dose at the same depth in the complete phantom. This difference is so small that it is probably satisfactory to use the depth dose from the tables as the exit dose. This is especially the case when the patient lies on a treatment table and the exit surface is backed by considerable material.

Comparison of 200 kv. and 1,000 kv. Doses. A comparison of skin, depth, and exit doses for 200 kv. and 1,000 kv. roentgen rays is of practical importance. In Figure 11, *A* are given curves showing the ratios of the depth doses at 1,000 kv. to those at 200 kv., for the same target-skin distance, 70 cm., and for different irradiated areas, when the skin dose in each case is 100 per cent. The 1,000 kv. doses are taken from Table IV; the 200 kv. doses, half-value layer 1.8 mm. copper, from work previously published from the Memorial Hospital.[35] As is to be expected, the improvement in depth dose at 1,000 kv. is much greater for small fields than for large, since in small fields the contribution of scattered radiation to the depth dose is less and the increased penetrating power of the primary beam is more significant. Values from these curves may be used directly in the determination of tissue doses, *provided the skin doses are the same*. At the present time, however, dosages are still often specified in terms of roentgens *in air*, and equal doses are con-

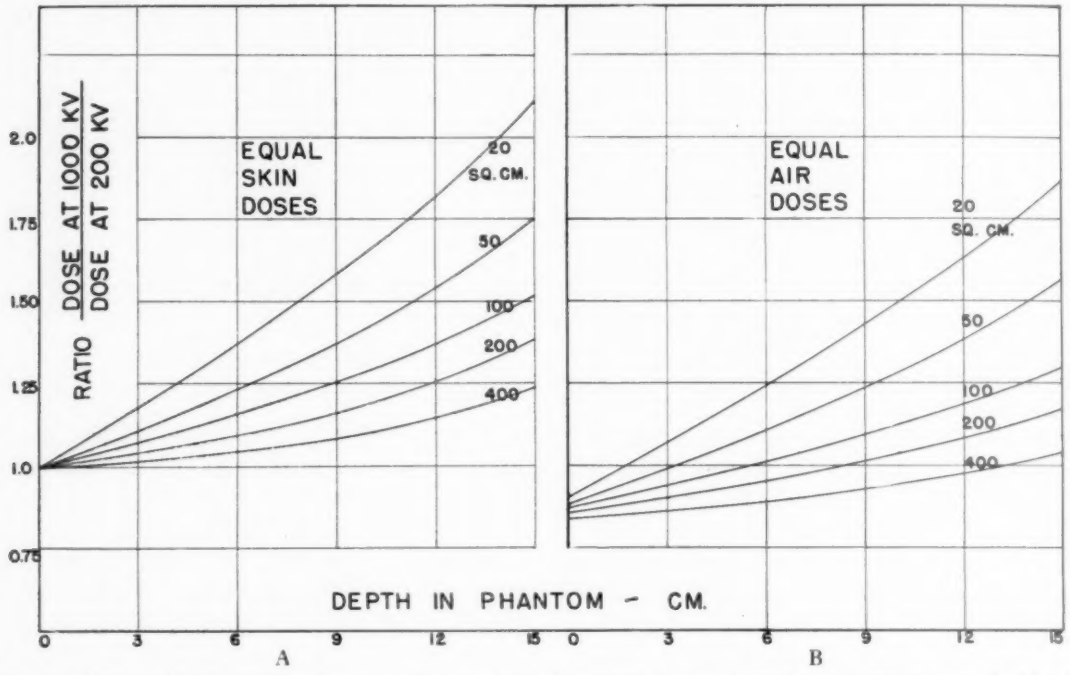


FIG. 11. Curves showing ratios between tissue doses for 1,000 kv. and 200 kv. roentgen rays (half-value layers 3.8 mm. Pb and 1.8 mm. Cu respectively); 70 cm. focal-skin distance.

sidered on this basis. In this case, the skin doses are not equal, because of the difference in backscatter, and the ratios of the tissue doses are those shown in Figure 11, *B*. In this case, it is seen that at, and near, the surface, the tissue dose is actually less for supervoltage radiation; the latter does not become equal to the 200 kv. dose until ential effect. It is therefore extremely important to investigate the matter more thoroughly. The Memorial Hospital 1,000 kv. machine cannot be operated at appreciably lower voltages; it was, accordingly, not possible for the present authors to determine directly whether the depth doses given above are or are not better than would

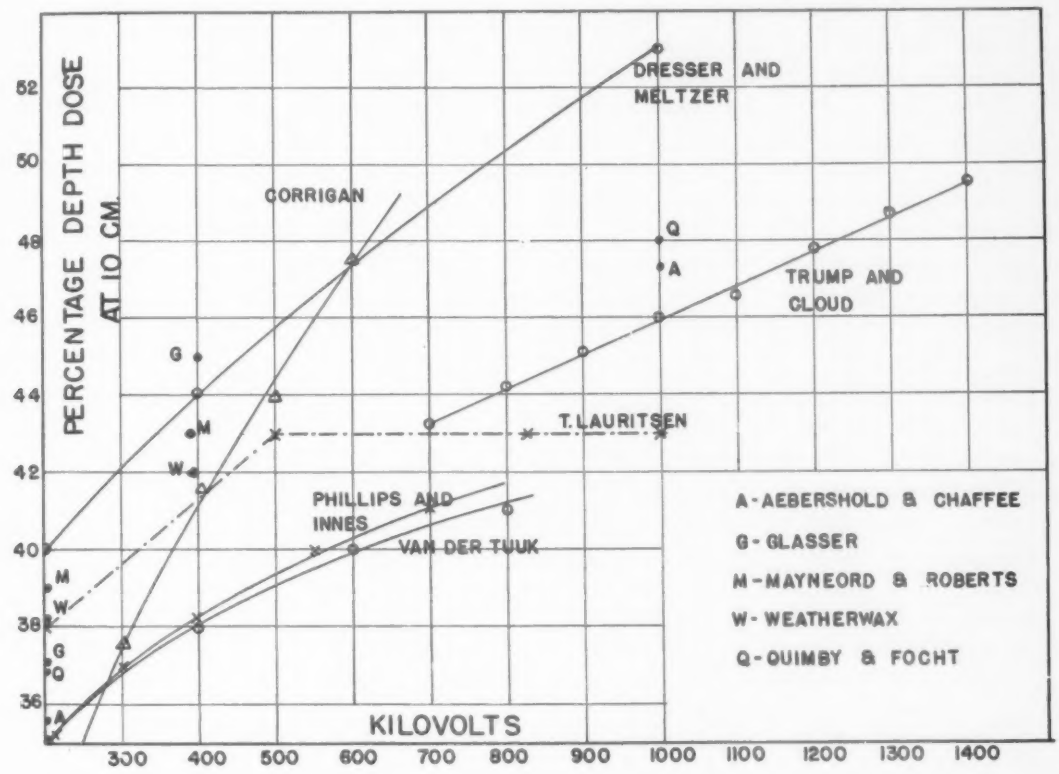


Fig. 12. Data showing variation in tissue dose at 10 cm. depth with variation in kilovoltage. (Collected from the literature.)

a depth of several centimeters is reached—3 cm. for a 50 sq. cm. field, and more than 10 cm. for one of 400 sq. cm.

It is sometimes stated that there is probably little or no gain in depth dose with increase in voltage beyond 300 or 400 kv.; in fact, T. Lauritsen[30] has published a paper giving the same percentage depth doses at 10 cm. over a range of voltage from 200 to 475 equivalent kilovolts (about 400 to 900 pulsating potential). If this were the case, the only advantage of higher voltages would lie in a possible wave length differ- have been obtained in the 400 kv. region. However, a study of published data by various workers throughout the voltage range under consideration is illuminating on this point. While, as stated above, few complete depth dose curves are available, there is a considerable amount of information on the depth dose at 10 cm. Corrigan,[6] Phillips and Innes,[33] van der Tuuk,[50] and Trump and Cloud[48] have published data covering a range of voltages between 200 and 1,400 kv.; Glasser,[20] Weatherwax,[51] and Mayneord and Roberts[32] contribute additional val-

ues for 200 and 400 kv., Aebersold and Chaffee,[1] Dresser and Meltzer[10] and the present paper for 200 and 1,000 kv. In Figure 12 are collected the 10 cm. depth doses given by the above mentioned authors, all corrected to 100 sq. cm. field and 70 cm. distance. (The actual distances employed varied from 50 to 100 cm.; the actual fields from 100 to 150 sq. cm. The necessary corrections were not large, and in any case would not change the shape of any of the curves, but only their position on the chart). The depth doses are plotted against kilovoltage. For any one voltage, there is a considerable variation in the percentage depth dose obtained by various workers, as might be expected in view of the variations in filtration, wave form, measuring method, etc. The important fact is that, with the single exception noted above, the data of each author show a constant upward trend as long as the voltage is increased, even up to 1,400 kv. From this collected information, the inescapable conclusion is that it is advantageous, from the point of view of increasing the percentage depth dose, to employ voltages as high as are yet available. It is to be regretted that most of the papers here quoted do not contain information for 15 cm. depths; at that level the advantage of higher voltages would doubtless have been shown to be even greater.

It must be remembered in this connection that, in order to obtain full advantage of higher voltages, adequate filtration must be employed, to suppress all the softer components of the beam. Phillips and Innes have shown that with light filtration there is little increase in depth dose at 10 cm. from 500 to 700 kv., whereas at 670 kv. the

TABLE V

COMPARISON OF TISSUE DOSES IN ROENTGENS

200 kv., Half-value Layer 1.8 mm. Cu. 1,000 kv., Half-value Layer 3.8 mm. Pb.
70 cm. Focal-skin Distance
Doses in Roentgens at Specified Points

Point	100 r of each *in air*		100 r of each *on incident field*	
	200 kv.	1,000 kv.	200 kv.	1,000 kv.
Midline of Neck 12 cm. in Diameter. 50 sq. cm. Field				
Air	100	100	83	94
Surface	121	107	100	100
Midline-one beam	63	71	52	66
Midline-two beams	126	142	104	132
Percentage gain for 1,000 kv.		12		27
Exit			25	37
Total skin			125	137
Midline-two beams for equal total skin			114	132
Percentage gain for 1,000 kv.				16
Midline of Pelvis 24 cm. in Diameter. 100 sq. cm. Field				
Air	100	100	80	91
Surface	126	110	100	100
Midline-one beam	38	45	30	41
Midline-two beams	76	90	60	82
Percentage gain for 1,000 kv.		19		37
Exit			5	12
Total skin			105	112
Midline-two beams for equal total skin			64	82
Percentage gain for 1,000 kv.				28

depth dose can be definitely increased by the addition of lead filters up to 3 mm. Corrigan's work, and that of Trump and Cloud confirm this. Since Lauritsen gives insufficient information regarding either his actual voltages or filtrations, it is not possible to suggest whether his lack of increase in depth dose with increase in voltage is due to underfiltration or to some other cause.

In analyzing the advantages in tissue dose of 1,000 kv. over 200 kv., such curves as those of Figure 11 are sufficient when single fields are employed, or in cross-fire when the exit field does coincide with the portal of entry of another beam. However, when the exit dose does act upon such a portal, the greater penetrating power of the 1,000 kv. rays may cause a significant increase in the skin dose which ought not to be neglected. To illustrate this point, calculations of the depth doses delivered by cross-fire at the midline of a neck and of a pelvis are tabulated in Table v, for equal air doses, for equal doses on the portal of entry, neglecting exit doses, and for equal total skin doses. As is evident from Figure 11 the advantage of 1,000 kv. is considerably less for equal air doses than for equal skin doses. When equal doses on the incident field only are considered and the exit dose neglected, the advantage of 1,000 kv. is, of course, the same as that shown in Figure 11, *A*. This is, however, not a fair basis of comparison for the actual case, since the actual total skin dose is greater for the 1,000 kv. radiation. When the exit doses are included, the advantage, while still definite, is somewhat less.

Stone and Aebersold, and Aebersold and Chaffee, have carried out a number of analyses of this type, for various practical cases. It is evident that such an analysis should be carried out for any particular case, before a decision is reached as to the relative desirability of the various methods. It is obvious that, whenever possible, skin field should be so chosen that portals of exit will not coincide with portals of entry.

An approximate analysis of the compositions of the radiation at various depths, for the two beams, is of interest, and can be made by a method developed by Friedrich and Körner,[19] and first extensively used by Dessauer and Vierheller[9] in 1921. It is necessary to know the rate of absorption of the primary beam in the phantom material. Absorption curves, made with a thimble chamber and a small beam, for the two qualities of radiation in pressdwood have been made. The analysis is developed. in Table vi. In column 1 is given the depth in the phantom. In columns 2 and 3 are given the percentage decreases in the primary beam due to the inverse square law and to absorption in pressdwood. The product of these in column 4 indicates the portion of the primary beam arriving at the specified depth. In column 5 are listed the number of roentgens arriving at the various levels, per 100 roentgens in air. These values are obtained by adding the backscatter to the air dose to give the skin dose, and then taking the percentage of this indicated in Table iv for the 1,000 kv. radiation, and in the previously mentioned data for 200 kv. The difference between these values and those in column 4 show the roentgens of scattered radiation (column 6), and the ratio of this to the total dose at any depth gives the percentage which is due to scatter, listed in column 7. The increased importance of scatter in large beams has long been recognized, since the depth dose at any level increases with the size of the beam whereas the portion of primary radiation reaching a given depth must be essentially the same. From Table vi it is evident that this increase in scatter with field is much less at 1,000 kv. than at 200 kv. This accounts for the fact, shown in Figure 11, that improvement in depth dose from 200 kv. to 1,000 kv. is much more marked for small fields than for large.

In any study of tissue dosage, the factor of focal-skin distance should be considered. The advantage of increasing distance on increasing percentage depth dose is well understood by radiologists in general; however, the statement is occasionally made that no such improvement is to be expected

TABLE VI

ANALYSIS OF ROENTGEN RAY BEAMS WITHIN THE PHANTOM FOR PRIMARY AND SCATTERED COMPONENTS
1,000 kv., Half-value Layer 3.8 mm. Pb, 70 cm. Focal-Skin Distance.
200 kv., Half-value Layer 1.8 mm. Cu, 70 cm. Focal-Skin Distance.

1 Depth	2 Inverse Square Factor	3 Absorption in Pressd-wood Factor	4 Per Cent Primary at Depth	5 Roentgens at Depth per 100 in Air	6 Scattered and Secondary Roentgens	7 Per Cent Scattered and Secondary in Beam
			20 sq. cm. field—200 kv.			
0	1.00	1.00	100	115	15	15
5	0.87	0.46	40	59	19	32
10	0.77	0.21	16	28	12	43
15	0.68	0.11	8	14	6	43
20	0.60	0.06	4	7	3	43
			20 sq. cm. field—1,000 kv.			
0	1.00	1.00	100	105	5	5
5	0.87	0.72	63	71.5	8	11
10	0.77	0.51	39	43	4	9
15	0.68	0.36	24.5	26.3	1.8	7
20	0.60	0.26	15.5	16.8	1.3	8
			100 sq. cm. field—200 kv.			
0	1.00	1.00	100	126	26	26
5	0.87	0.46	40	84	44	52
10	0.77	0.21	16	47	31	66
15	0.68	0.11	8	28	20	71
20	0.60	0.06	4	14	10	72
			100 sq. cm. field—1,000 kv.			
0	1.00	1.00	100	110	10	10
5	0.87	0.72	63	84	21	25
10	0.77	0.51	39	53	14	26
15	0.68	0.36	24.5	33	8.5	27
20	0.60	0.26	15.5	22	6.5	29
			400 sq. cm. field—200 kv.			
0	1.00	1.00	100	136	36	36
5	0.87	0.46	40	106	66	63
10	0.77	0.21	16	65	51	78
15	0.68	0.11	8	40	32	80
20	0.60	0.06	4	22	18	82
			400 sq. cm. field—1,000 kv.			
0	1.00	1.00	100	115	15	15
5	0.87	0.72	63	92	29	32
10	0.77	0.51	39	61	22	36
15	0.68	0.36	24.5	41	16.5	40
20	0.60	0.26	15.5	28	12.5	44

on theoretical grounds.[29] Such statements are not supported by experimental evidence. In the 200 kv. region it has been repeatedly demonstrated that, when the irradiated area is kept constant, the increase in percentage depth dose is such as would be predicted on a basis of the inverse square law.[19,21,34] In the course of the measurements reported in the present paper, this was verified incidentally for shifts in dis-

tance from 50 to 70 cm.; it was not considered necessary to study the matter in detail. However both Phillips and Innes, and Trump and Cloud have investigated the question for ranges of distances from 50 to 100 cm., the latter authors having made their measurements over a range of voltages from 700 to 1,400 kv. Data from both these papers show consistent increase in percentage depth dose with focal-skin distance. Trump and Cloud conclude, "The gain is about as great as might be deduced from a simple consideration of the inverse square law."

The Erythema Dose. All the foregoing data are based on physical measurements. Equal numbers of roentgens mean equal numbers of ions per gram of air, under proper conditions of measurement. One hundred per cent on the skin does not mean one erythema dose, or any other biological unit. The question immediately arises, therefore, as to the possible difference in biological or clinical effect with these two qualities of radiation under discussion. Especially is the tolerance of the skin important. If it will tolerate a larger quantity of the supervoltage radiation than of the 200 kv. rays, the advantage of the former due to increased penetration can be still further improved upon. Of course, if the skin tolerates more of the penetrating radiation, it is not certain whether other tissues will also, or whether various tissues will have different tolerance ratios. This can only be determined by observation in actual treatments.

The skin erythema dose can, however, be determined by direct experiment. The so-called threshold dose for 200 kv. roentgen rays, for a region on the skin of the forearm, has previously been found to be 650–700 r, measured on the skin.[11,31] The corresponding dose for gamma rays is in the neighborhood of 1,000 r$_\gamma$.[36] It would be expected that for 1,000 kv. roentgen rays it would lie between these two. Accordingly skin tests were commenced with 800 r on the skin, and carried up to 1,200 r, with very few visible reactions. Of five tests at 1,000 r (skin) only one showed a definite reaction, and of nine at 1,100 r, three were negative or doubtful.

At this point, the suggestion was made by Dr. Failla that the number of roentgens measured with a thick-walled ionization chamber probably did not represent the ionization at the level of the cells involved in the production of the skin reaction.

The situation represents a condition analyzed in a paper by Failla, Twombly and Marinelli[16] on a method for decreasing the ionization in the skin, applicable to supervoltage therapy, but not attainable by them at the time of their experiments, because no suitable supervoltage installation was available.

When the roentgen-ray beam leaves the collimating diaphragm (see Fig. 1) it is probably heavily loaded with secondary electrons from the tube container, diaphragms, etc. The energy of many of these electrons is such that if they started toward the skin, and were not interfered with, many of them would reach it. However, few of them are not interfered with. As they undergo collisions with gas atoms of the air, they are deflected from their original paths, and as a result many are sent completely outside the beam and do not return to it. This happens to a larger percentage of the electrons in small beams than in large, but for 1,000 kv. radiation and distances from the diaphragms of the order of 50 cm., a significant portion are removed even from fairly large therapy beams. Some secondary electrons, of course, arise from the action of the roentgen rays upon the air within the beam; a part of these also are deflected out of the beam and never reach the skin. However, when the beam enters the tissue, since this is much denser than air, a vastly greater number of electrons begin to be contributed, and these, travelling much shorter distances in tissue than in air, do not leave the beam. The building up of the electron content of the beam goes on, with increasing depth, until electron equilibrium or compensation is reached. At this point the ionization in a very tiny volume of air

at the center of the beam is the same as the total ionization produced by all the secondary electrons liberated in that volume; this condition persists as the beam goes into the body. The depth at which equilibrium is established depends on the range in tissue of the secondary electrons, which, in turn, depends on the quality of the primary beam. For 200 kv. roentgen rays it is only a very small fraction of a millimeter; for 1,000 kv. the maximum range of the secondary electrons is in the neighborhood of 4 mm.[13] Only a very few travel this maximum distance, but in Part I of this paper it has been shown that a thickness of 1.5 mm. of unit density organic material is necessary to establish electron equilibrium inside a thimble chamber. It may be assumed, on this basis, that equilibrium is essentially established at this depth within the body. In layers of tissue less deep than this, the electron content of the beam is less than the equilibrium amount. If the cells involved in erythema production lie in these superficial layers, the radiation reaching them is the same as that in the extrapolation chamber when the upper electrode is thinner than the maximum, corresponding to the situation illustrated in Figure 2. The ionization actually produced in these cells is then not equal to that in a thick-walled chamber, but something less. For this reason, skin reactions were not appearing at the dosage which had been calculated to be in the proper range. The clinical implications of this fact will be discussed below.

If this is the case, placing enough organic material on the skin surface to bring the total depth of the cells in question to 1.5 mm. should result in the production of a reaction. Accordingly, half the skin field was covered with a few layers of rubber dam,* and tests made as before. Three tests at 1,100 r now showed definite reactions under the rubber, with slight or no effect on the exposed portion. Five tests at 1,000 r showed the reaction under the rubber; two of these had visible reactions on the exposed portion; the others were questionable. Of three tests at 900 r, two were completely negative, one showed reaction under the rubber but not on the exposed area. It is evident that the dose corresponding to the threshold erythema dose for other qualities of radiation is very close to 1,000 r. It should be noted that it is more difficult to determine the limiting dose at 1,000 kv. than at 200 kv. A true erythema is practically never noted for the doses specified. The visible reaction is the tanning which appears three to six weeks after the irradiation. This may be very faint, so that one experienced in looking for such reactions can detect it, but it would otherwise pass unnoticed. Several observers saw each patient at various times. Each made his own decision as to the reaction. The results of tests here reported represent the consensus of these observers.

There are few data in the literature on the subject of the skin reaction in this voltage region. Stone[43] compared skin reactions for 1,000 kv. and 200 kv. under conditions of divided dose therapy. He made very few tests for single exposures. He does report that 800 r measured in air produced no reaction on fields 10×10 cm. on hip, shoulder, or abdomen; 1,000 r (air) produced a marked reaction on a 15×15 cm. field on the lower abdomen. These doses correspond to skin doses of 900 and 1,125 r, if complete electron compensation exists at the level of the involved cells; the findings are, accordingly, what would be expected on the basis of the data reported above. In Stone's tests the air dose was measured with a Victoreen ionization chamber. A treatment cone was employed, with a closing cover of felt and aluminum, so that the skin should have been receiving the dose indicated by the chamber, plus the correct backscatter.

At the Swedish Hospital in Seattle, with roentgen rays generated at about 800 kv., the open port method is employed, so that

* The possibility of the presence of elements of higher atomic weight in the rubber must not be overlooked. Through the courtesy of the Davol Rubber Company, the composition of the rubber employed was obtained. Very small amounts of sulfur and of zinc were present. However the effective atomic number is somewhat less than that of tissue.

the reactions obtained should agree with those at Memorial Hospital when no cover is placed on the skin. We were informed that 1,000 r measured in air is considered the threshold dose; this is in general agreement with the observations mentioned above.[3]

In 1933, Lauritsen[28] published a theoretical curve showing the variation in the number of roentgens required to cause absorption of 1.4×10^4 erg per sq. cm. of surface layer 1 mm. thick. He states that a curve of erythema doses can be expected to be similar, provided there is no biological wave length effect. Since this curve is plotted in terms of kilovolts to produce monochromatic radiation, it is difficult to compare it with actual roentgen-ray beams. However, on a basis of absorption data it may be considered that the 200 kv. radiation employed at the Memorial Hospital is approximately equivalent to 100 kv. on his scale, and the 1,000 kv. to approximately 600 kv. For a voltage increase of from 100 to 600 kv., the calculated number of roentgens required to produce an erythema is more than doubled. Experimentally this does not prove to be the case, as has already been pointed out by Stone. At 200 kv. (pulsating) he found, as stated above, that 650–700 r produced the threshold reaction, and at 1,000 kv., 950–1,000 r, which is an increase of the order of 50 per cent rather than of 100 per cent.

It appears, accordingly, that the theoretical curve should be considered as indicating an expected trend in erythema doses, rather than as providing a clinically applicable set of data. As a matter of fact, the curve seems to have been applied by others more closely than Lauritsen intended. It should be pointed out that actually what he has calculated is a first approximation to the air dose plus the backscatter, for a very wide beam. The rigorous mathematical determination of this quantity is practically impossible, because of the complicated nature of the scattering processes in an extended medium, hence it is necessary to make assumptions regarding these. Such assumptions lead to results which are of value for purposes of understanding the processes involved, but which are, of necessity, more or less inaccurate. The assumptions which Lauritsen has made as to the contribution of the backscatter to the radiation effective at the skin are very broad, and not closely applicable to the conditions of therapy. When it is understood that this curve is intended to represent solely air dose plus backscatter, this inconsistency becomes apparent. An increase in the required air dose of 100 per cent between 200 and 1,000 kv. implies an equal decrease in backscatter, if biological wave length effects are not considered. This means that, if the backscatter at 1,000 kv. is assumed to be negligible, that at 200 kv. must be 100 per cent. This, of course, is contrary to experience.

A word should be said with regard to the possible clinical significance of the observed skin reactions. Although radiologists do not hesitate to push therapeutic doses to the point of very severe skin reactions, it is obviously an advantage to keep them as low as possible, compatible with the administration of an adequate dose to the deeper tissues. From this point of view, the use of open ports, and consequent removal of secondary electrons from the beam, with diminished skin reactions, is desirable. The accurate positioning of the patient may be slightly more difficult with open ports than with cones, but can be attained with the use of reasonable care. If the intensity of the beam is high, so that the individual treatments are short, the patients can readily be kept in the desired position for the necessary interval. The use of an integrating dosimeter on the skin gives additional assurance with regard to this. However, it must be remembered that the dosimeter, or anything else on the skin, will contribute electrons. A chamber occupying an appreciable part of the skin field might nullify much of the advantage of the open port, which is greatest for small beams.

It should be pointed out that this effect has no significance in the 200 kv. region. The paths of the secondary electrons in

tissue are so short that equilibrium is attained before the radiation reaches the level of the cells concerned with skin reaction.

It is true that under these conditions a statement of the skin dose in roentgens (implying for 1,000 kv. the use of a thick-walled ionization chamber) does not actually specify the number of ions being produced at the level of the cells presumably responsible for the erythema effect. For this reason when skin doses in terms of roentgens are discussed, the statement as to cone or open port should always be made, so that variations in skin response to supposedly equal doses will be understood.

It should also be mentioned that such variations have been studied only in the production of threshold reactions. No observations have been made under actual conditions of therapy. With high dosage and marked reactions, the effect of covering material will probably be less marked.*

SUMMARY AND CONCLUSIONS

Preliminary studies on suitable ionization chambers for measurement of supervoltage roentgen rays indicate the need of a wall thickness of about 1.5 mm. of unit density air-wall material.

Absorption curves in various substances, made with such a chamber, for 1,000 kv. roentgen rays, are presented.

Data published by other workers throughout the voltage range from 400–2,000 kv. are collected and correlated in studies of half-value layers in lead, copper, and tin. It is concluded that there is no advantage, but rather a disadvantage, in changing from copper to tin as the metal for half-value layer specifications above 400 kv. It is suggested that either the change be made from copper to lead at about 700 kv., or that copper be employed throughout the entire voltage range above 120 kv.

Backscatter and depth dose data are presented for 1,000 kv. roentgen rays, for a 70 cm. focal-skin distance and a wide range of fields.

Extensive comparisons are made between these doses and the corresponding ones for 200 kv.

Because the statement is sometimes made that there is probably little or no gain in percentage depth dose with voltage increase above 300 or 400 kv., information has been collected from the literature on depth doses throughout the voltage range from 400 to 1,400 kv., and correlated to examine this point. It is concluded that, throughout the region studied, the depth dose at 10 cm. or more continues to increase definitely with increase in voltage.

The percentage depth dose has been shown to increase with focal-skin distance in accordance with the inverse square law.

The threshold skin erythema dose for 1,000 kv. roentgen rays has been determined to be about 1,000 r when the roentgen rays are in equilibrium with their secondary electrons at the surface of the skin.

It is shown that with 1,000 kv. roentgen rays, for a given number of roentgens in air, the skin reaction can be decreased by the use of an open port and the omission of any sort of material covering the skin. This is due to the fact that under these conditions the roentgen-ray beam arrives at the skin surface with less than its equilibrium quota of secondary electrons, and that complete electron compensation is not attained until a depth in tissue greater than that of the cells producing the erythema reaction. This is not the case with radiation in the 200 kv. range.

The authors take pleasure in acknowledging their indebtedness to other members of the laboratory staff, Mr. Marinelli, Mr. Folsom, and Mr. Walke, for their generous cooperation in this study.

REFERENCES

1. AEBERSOLD, P. C., and CHAFFEE, M. A. Practical considerations in comparison of depth doses achieved by 1,000 and 200 kilovolt x-ray apparatus. *Radiology*, 1939, *33*, 759–767.

* July, 1941. In some therapeutically treated cases, half the field has been regularly covered with rubber dam, the other half left uncovered. The reaction in the skin that had been covered was always more marked than in the uncovered portion.

2. BOUWERS, A., and VAN DER TUUK, J. H. A new x-ray tube for 700 k.v. and some measurements of penetrating radiation. *Brit. J. Radiol.*, 1936, *9*, 431–441.
3. CANTRIL, S. T. Personal communication.
4. CHAO, C. Y. Scattering of hard γ-rays. *Phys. Rev.*, 1930, *36*, 1519.
5. CHARLTON, E. E., WESTENDORP, W. I., DEMPSTER, L. E., and HOTALING, G. A new million volt x-ray outfit. *J. Applied Physics*, 1939, *10*, 374.
6. CORRIGAN, K. E. Comparison of the effect of various filters in the 500 kv. range. AM. J. ROENTGENOL. & RAD. THERAPY, 1937, *37*, 520–528.
7. CORRIGAN, K. E., and CASSEN, B. Spatial distribution of radiation from a supervoltage roentgen tube and its significance in therapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1937, *37*, 811–818.
8. CUYKENDALL, T. R. Absorption of x-rays of wave-length $50 \leqq \lambda < 150$ X.U. by elements of low atomic number. *Phys. Rev.*, 1936, *50*, 105.
9. DESSAUER, F., and VIERHELLER, F. Die Tiefenwirkung der Röntgenstrahlen. *Strahlentherapie*, 1921, *12*, 655–690.
10. DRESSER, R., and MELTZER, A. Effect of heavy filtration on skin tolerance and depth dose. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *42*, 756–759.
11. DUFFY, J. J., ARNESON, A. N., and VOKE, E. L. Rate of recuperation of human skin following irradiation. *Radiology*, 1934, *23*, 486–490.
12. FAILLA, G. A new instrument for measuring x-radiation. *Radiology*, 1930, *15*, 437–448.
13. FAILLA, G. Versuch einer neuartigen Therapie mit überharten Röntgenstrahlen. *Strahlentherapie*, 1936, *56*, 594–602.
14. FAILLA, G. Measurement of tissue dose in terms of the same unit for all ionizing radiations. *Radiology*, 1937, *29*, 202–215.
15. FAILLA, G., and MARINELLI, L. D. Measurement of the ionization produced in air by gamma rays. AM. J. ROENTGENOL. & RAD. THERAPY, 1937, *38*, 312–343.
16. FAILLA, G., TWOMBLY, G., and MARINELLI, L. D. A method for decreasing the ionization in the skin applicable to supervoltage x-ray therapy. *Radiology*, 1937, *28*, 693–703.
17. FOLSOM, T. R. Some physical aspects of the 650 kv. constant potential x-ray apparatus at the Lincoln General Hospital. *Radiology*, 1936, *27*, 679–688.
18. FRIEDRICH, W. Measurement of gamma rays. AM. J. ROENTGENOL. & RAD. THERAPY, 1938, *40*, 69–79.
19. FRIEDRICH, W., and KÖRNER, H. Experimental investigations of the influence which the focus skin distance and the size of the field have on the quotient of the dose. Principles of Physics and Biology of Radiation Therapy. Krönig and Friedrich. Rebman Co., New York, 1922, p. 209. Translated and reprinted from *Strahlentherapie*, 1920, *11*, 961–979.
20. GLASSER, O. Dosage measurements on ten 400 kv. roentgen-ray generators. AM. J. ROENTGENOL. & RAD. THERAPY, 1937, *38*, 769–775.
21. GREBE, L., and NITZGE, K. Tabellen zur Dosierung der Röntgenstrahlen. Sonderbände zur Strahlentherapie, Band XIV. Urban und Schwarzenberg, 1930.
22. HERRMANN, H., and JAEGER, R. Ueber den Strahlenschutz bei harten Röntgenstrahlen. *Strahlentherapie*, 1931, *41*, 321–328.
23. HUDSON, J. C. Physical measurements on roentgen radiation from a tube actuated by a Van de Graaf generator. *Radiology*, 1939, *32*, 530–537.
24. INTERNATIONAL COMMITTEE FOR RADIOLOGICAL UNITS. Recommendations, Chicago, 1937. *Radiology*, 1937, *29*, 634.
25. JONES, M. T. The absorption of ultra-short x-rays by elements of high atomic number. *Phys. Rev.*, 1936, *50*, 110.
26. KAYE, G. W. C., and BINKS, W. Ionization measurement of gamma radiation. AM. J. ROENTGENOL. & RAD. THERAPY, 1938, *40*, 80–91.
27. LAURITSEN, C. C. Energy consideration in high voltage therapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1933, *30*, 380–387.
28. LAURITSEN, C. C. Energy considerations in medium and high voltage therapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1933, *30*, 529–532.
29. LAURITSEN, C. C. Development of high voltage x-ray tubes at the California Institute of Technology. *Radiology*, 1938, *31*, 354–361.
30. LAURITSEN, T. Depth dose measurements with a 1,000 kv. roentgen tube. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *41*, 1003–1006.
31. MACCOMB, W. S., and QUIMBY, EDITH H. Rate of recovery of human skin from effects of hard or soft roentgen rays or gamma rays. *Radiology*, 1936, *27*, 196–207.
32. MAYNEORD, W. V., and ROBERTS, J. E. The ionization produced in air by x-rays and gamma rays. *Brit. J. Radiol.*, 1934, *7*, 158–175.
32*a*. NAIDU, R. Ionization in air and in gas mixtures approximating composition of tissues. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *41*, 992–998.
33. PHILLIPS, R., and INNES, G. S. Physical measurements in high voltage-x-ray therapy. *Brit. J. Radiol.*, 1938, *11*, 498–503.
34. QUIMBY, EDITH H. The use of long target-skin distances in roentgen therapy. AM. J. ROENTGENOL. & RAD. THERAPY, 1936, *36*, 343–349.
35. QUIMBY, EDITH H. Syllabus of Lectures on the

Physical Basis of Radiation Therapy. Edwards Bros., Ann Arbor, Mich., 1939.
36. QUIMBY, EDITH H. The specification of dosage in radium therapy. AM. J. ROENTGENOL. & RAD. THERAPY, Jan., 1941, *45*, 1–16.
37. QUIMBY, EDITH H., and LAURENCE, G. C. Radiological Society of North America Standardization Committee. Technical Bulletin no. 1. *Radiology*, 1940, *35*, 138–159.
38. QUIMBY, EDITH H., and MARINELLI, L. D. Unpublished work.
39. QUIMBY, EDITH H., MARINELLI, L. D., and FARROW, J. H. A study of back-scatter. AM. J. ROENTGENOL. & RAD. THERAPY, 1938, *39*, 799–815.
40. READ, J. Absorption of monochromatic x-ray beams of wave length in the region 50 to 20 x-units in lead, tin, copper, and iron. *Proc. Roy. Soc.*, 1935, *152*, 402.
41. READ, J., and LAURITSEN, C. C. Investigation of the Klein-Nishina formula for x-ray scattering in the wavelength region 50 to 20 x-units. *Phys. Rev.*, 1934, *45*, 433.
42. ROSE, J. E. Personal communication.
43. STONE, R. S. Skin reactions caused by 1,000 kilovolt and 200 kilovolt radiations. *Radiology*, 1938, *30*, 88–93.
44. STONE, R. S., and AEBERSOLD, P. C. Clinical deductions from physical measurements of 200 and 1,000 kilovolt x-rays. *Radiology*, 1937, *29*, 296–304.
45. STONE, R. S., LIVINGSTON, M. S., SLOAN, D. H., and CHAFFEE, M. A. A radiofrequency high voltage apparatus for x-ray therapy. *Radiology*, 1935, *24*, 298.
46. TAYLOR, L. S., SINGER, G., and CHARLTON, A. L. Measurement of supervoltage x-rays with free-air ionization chamber. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *41*, 256–275.
47. TAYLOR, L. S., and SINGER, G. Measurement, in roentgens, of gamma radiation from radium by free-air ionization chamber. *J. Research, Nat. Bur. Standards*, March, 1940. Research paper RP1283.
48. TRUMP, J. G., and CLOUD, R. W. Physical characteristics of supervoltage roentgen rays. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *44*, 615–618.
49. VAN ATTA, L. C., and NORTHRUP, D. L. Measurements of roentgen-ray production in the range 0.8 to 2.0 million volts. AM. J. ROENTGENOL. & RAD. THERAPY, 1939, *41*, 633–636.
50. VAN DER TUUK, J. H. Messungen an Röntgenstrahlen bis 1 million Volt. *Fortschr. a d. Geb. d. Röntgenstrahlen*, 1938, *58*, 83.
51. WEATHERWAX, J. L. Personal communication.
52. WHITE, T. N., MARINELLI, L. D., and FAILLA, G. A measurement of gamma radiation in roentgens. AM. J. ROENTGENOL. & RAD. THERAPY, 1940, *44*, 889–903.

DISCUSSION ON PAPERS BY DRS. TAFT, AND QUIMBY AND FOCHT

DR. RICHARD DRESSER, Boston. I have been very much interested in the subjects that have been presented and it is a pleasure to have the opportunity to discuss them.

About three and a half years ago when we first started therapeutic work with apparatus operating at 1,000 kv., we were naturally interested in protection against the short wave lengths thus produced. A chamber was constructed similar to that which is now commerically available from the Victoreen Instrument Company. I will present briefly the conclusions that were arrived at.

It was found that 6 inches of lead were necessary to stop the direct radiation produced at 1,000 kv.; however, 1 foot of cement gave entirely adequate protection against the scattered radiation.

Comparative measurements were made on lower voltage apparatus, and it was found that the intensity of scattered radiation from a commercial shockproof unit, operated at 200 kv., was approximately twice that from the 1,000 kv. unit; however, ¼ inch of lead proved to be sufficient to give adequate protection from 200 kv. radiation both direct and scattered.

Measurements similar to those which Dr. Taft has presented showed that the intensity reaching the operator during roentgenoscopy might be 1/100 of a roentgen per minute.

Now, as to Dr. Quimby's paper:

(Slide) I have made comparative measurements between 200 and 1,000 kv. roentgen rays, using the same distance which Dr. Quimby has employed, and the same set of factors all the way through.

It is important to note the difference in output between the 200 kv. unit, operating at full capacity and the 1,000 kv. unit also operating at capacity. Twenty-five r per minute is obtainable at the lower voltage at a distance of 70 cm. with a filter of 0.5 mm. copper. At the higher voltage it is possible to get 140 r per minute at a distance of 70 cm. with filtration of 3.5 mm. of lead and 8 mm. of copper. At the higher potentials the intensity tends to go up as the cube of the voltage rather than the square of the voltage.

The surface backscatter from superhard radiation is one-third that observed with 200 kv. rays when large portals of entry are employed. It is reduced to approximately one-quarter

when small fields are used. It is well known that the depth dose from 200 kv. radiation falls off markedly with decrease in the size of field. At 1,000 kv. this decrease with change of portal becomes almost negligible.

Dr. Otto Glasser, Cleveland, Ohio. Dr. Taft's presentation is of great importance. We have made protection measurements before and have seen them reported in the journals, but I think it is very timely to call attention again and again to the danger of overexposure from stray radiation. At the present time we are not even certain that one-tenth of one roentgen is a safe tolerance dose. New work done at the Massachusetts Institute of Technology, and also by a number of workers in genetics seems to prove that we probably should reduce the tolerance dose to one-hundredth of a roentgen per day.

Unfortunately, today there are still many installations in this country where the operator is not properly protected against stray radiation, and I speak from experience. Within the last year I have inspected several places where the tolerance dose at the operator's desk was exceeded by at least several hundred per cent. This applied especially to old installations which have been changed from low voltage to higher voltage machines without adequate change in the protection.

One word of warning: It is almost unbelievable how much stray radiation can be gotten from some of the old type fluoroscopes; and furthermore, often the direct radiation the patient receives on the fluoroscopic table is far higher than expected. I would like to mention one example: In the past year a fluoroscopic unit was installed in an emergency ward in a large hospital which was used mostly to set fractures. I measured the amount of radiation which the patient received and found that 300 roentgens were applied in one minute. This result caused considerable surprise to the surgeons, who in many cases worked on a patient fifteen or twenty minutes. An additional filter of 0.5 mm. of aluminum solved the problem. For that reason do not be satisfied with vague protection data, but measure your stray and direct radiation.

Dr. Quimby has presented valuable data obtained on a million volt machine as compared with those of a 200 kv. generator. We are looking forward to this kind of report to arrive at a better foundation for discussion of the merits of supervoltage therapy. An important part of her paper describes the peculiar effect appearing on the skin when using supervoltage rays. It is interesting to note that if you add artificial tissue by any means over the skin and then irradiate it, the peculiar skin effect disappears.

Dr. Taft (closing). I have made no tests on spot filming. However as the voltage is generally the same as that used for fluoroscopy with about ten times the milliamperage, the dose would be ten times as great in the same time.

I am glad to have the information supplied by Dr. Dresser on voltages above 200,000. I have made no such tests as I have no such equipment.

In regard to the matter as to whether one-tenth of a roentgen per day is really a safe dose, I cannot, of course, definitely answer that. We accept for the present the statement made in the recognized handbooks on roentgen-ray and radium protection. These may not be right but we must accept them until someone shows us something better.

Nothing new was presented in this paper but if it has made you more mindful of the matter of protection, I feel that our time has been well spent.

Dr. Quimby (closing). The questions which have been raised as to method and data will be answered in the complete paper as published.

With regard to the matter of differential action, Dr. Glasser says he thinks the evidence against it is now complete that when the skin is covered so that we have equilibrium at the skin surface for all qualities of radiation, we then have no differential action. This is not the case. When equilibrium is established at the skin surface, and when variations in backscatter with variations in quality of radiation are taken into account, we still find that for 100 kv. roentgen rays the threshold erythema dose in *roentgens delivered to the skin* is about 300 r; for 200 kv., about 650 r; and for 1,000 kv., about 1,000 r. This difference is almost certainly due to biological rather than physical factors; in other words, it is a differential effect.

STABILITY OF THE STANDARD DOSAGE-EFFECT CURVE FOR RADIATION

By C. I. BLISS
Guest Investigator, U.S. Fish and Wild Life Service Laboratory
WOODS HOLE, MASSACHUSETTS
and
CHARLES PACKARD
Department of Cancer Research, Columbia University
NEW YORK, NEW YORK

IN MOST biological assays designed to test the potency of an active agent or drug, the mean susceptibility of the test animal varies to such an extent that a curve showing the relation between dose and effect, in one experiment, cannot be used safely in a later experiment. It is necessary, therefore, in each repetition to compare the reaction of the test animals to an agent of unknown potency with their reaction to a stable preparation of the same agent. An outstanding exception to this rule is the percentage survival of *Drosophila* eggs following exposure to the radiation of roentgen rays and of radium. One of us[3] has used a standard curve technique in many radiation studies and over a period of years many measurements have been made with the same roentgen-ray equipment under standard conditions. Since nearly two-thirds of these percentages were based upon 200 or more eggs and only 2 per cent upon less than 100 eggs, their sampling errors were relatively small and the data well suited for a critical test of the stability of the standard curve under uniform conditions.

The observations in the present study were obtained with a tube operating at 120 kv. through a filter of 0.25 mm. of copper and 1 mm. of aluminum with the half-value layer of the beam equal to 0.33 mm. of copper. The intensity of the radiation directed upon the eggs, placed at 30 cm. from the tube, ranged from 14.6 to 31.8 roentgens per minute as measured by a Victoreen dosimeter. The length of exposure was varied from 2 to 20.9 minutes, giving a dosage range of 61 to 500 roentgens.

The present experiments cover a period from November, 1930, to January, 1938, and include every record over this period showing a high fertility in the control eggs not exposed to irradiation, and room temperatures between 20° and 25° C. The flies were inbred wild-type *Drosophila melanogaster* of stocks originally from Oregon and from Florida, replaced by an "isogamic" stock in the last two months of testing. The sterility of 34 Oregon controls averaged 3.27 ±0.22 per cent of unhatched eggs, that of 20 Florida controls 3.27 ±0.29 per cent and of the 4 isogamic controls 3.08 ±0.66 per cent, the three stocks agreeing satisfactorily with the general mean of 3.26 ±0.17 per cent for all 58 controls.*

The variation between separate controls fell short of that expected from the binomial distribution. The deviations from the mean sterility of 3.26 per cent represented such close agreement that it would not be expected to occur by chance even once in 100,000 similar studies, as shown by $\chi^2 = 18.389$ with 57 degrees of freedom. No single mortality exceeded 5.4 per cent although four or five larger values would be expected among the 58 lots of control eggs. Presumably the elimination of all experiments where the controls did not meet a predetermined level has rejected a small though significant number of valid tests, but their omission would not bias the results from the treated eggs. The percentage of each irradiated lot to hatch was divided by 0.97 to correct for the mortality in the controls.

* Values following the ± signs are standard errors, enclosing about two-thirds of the expected variation in the term preceding the sign.

In all, 191 sets of eggs were irradiated under the above standard conditions. These data have been divided into 21 series of 5 to 15 sets, usually covering relatively short periods of time. In 14 series the elapsed time fell within a week but in 5 series it exceeded two months. When the data for all series were plotted in terms of percentage survival on the ordinate against the dose in roentgens along the abscissa, they described the asymmetrical sigmoid curve shown in Figure 1, which is similar to the standard curve reported in an earlier paper.[3] The data cannot be handled readily in this form, nor can the component 21 curves be compared critically. It is a simple matter, however, to transform them into straight lines on the assumptions that proportional increases in dose produce equal increments in effect and that variations in the susceptibility of eggs to irradiation are consistent with the normal curve of error. These relations lead necessarily to a straight line when dosages in roentgens (divided by 100

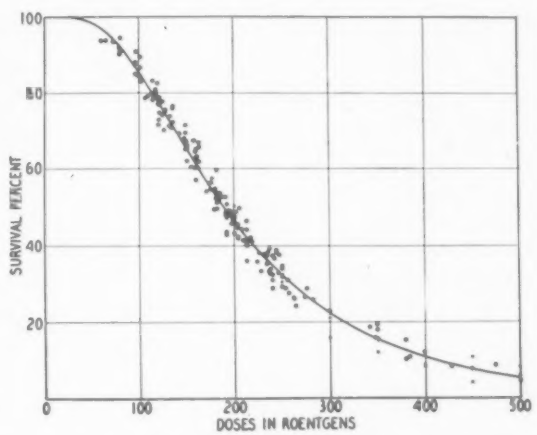


Fig. 1. Standard dosage survival curve of *Drosophila* eggs exposed to roentgen rays under conditions mentioned in the text.

to reduce arithmetic) are changed to logarithms (x) and percentage survivals to a function of the normal curve known as the "probit" (y) as shown in Figure 2. The probit is defined as the deviate of the normal curve in units of standard deviations plus 5 and tables are available[2] for converting percentages directly to probits. Graphic analysis of the separate series led to a single provisional curve representing all series, with the equation $y = 6.084 - 3.96x$. This agreed closely with the standard curve of $y = 6.101 - 3.96x$ obtained by an equivalent graphic technique and used for several years by one of us[3] in estimating dosage from percentage survival.

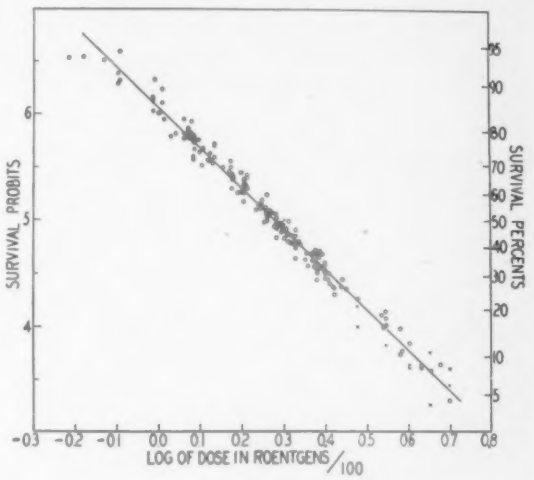


Fig. 2. Dosage survival curve of Figure 1 plotted in terms of logarithms and probits.

With the aid of the current provisional equation, from which the expected survival in probits could be computed for each set of eggs, the data for each of the 21 series were fitted with a separate curve by the efficient statistical technique known as the method of maximum likelihood. The calculation followed the procedure described elsewhere in detail,[1] the expected probits permitting the determination of the corrected probit for each observation and a weight proportional to the information it contained. Thus the use of more eggs in obtaining some percentage survivals than in others and the greater reliability of lots approaching equal survivals and deaths could be given due weight. Having determined the best-fitting curve for each series, the question at issue is whether these 21 curves agreed satisfactorily, first, with their basic observations and secondly, with each other within their sampling errors.

Agreement between individual observations and their respective curves was tested by computing the statistic χ^2 for each series. Tables are available showing how often the discrepancy represented by any observed χ^2 could have been obtained by chance if the observations agreed in fact with the curve. The use of these tables depends upon the degrees of freedom (n) for each χ^2, which here are equal to the number of observations minus 2. Cases where χ^2 exceeds that expected once in 20 times (expressed as $P=.05$) if the divergence were due to chance alone are generally considered to be significantly heterogeneous. In 19 of the present 21 series the observations were fitted satisfactorily by their respective curves, P varying from 0.23 to 0.92 and the χ^2 for all curves totalling 115.38 with $n=139$; in the remaining 2 series, each having 5 degrees of freedom, the observed χ^2's of 13.67 and 22.03 would indicate a clearly significant heterogeneity about the fitted lines ($P=.018$ and $<.001$) if obtained from isolated curves. In the present case, however, they are the extreme values in a series of 21 curves, among which one would expect to find by chance alone one or two series with χ^2's exceeding that expected once in 20 times. Considering all of the variation about the 21 individual curves, $\chi^2=151.077$ with $n=149$, indicating a fully adequate homogeneity.

The observations for the apparently heterogeneous series, however, together with one homogeneous curve, were obtained on a single day (January 26, 1933). Not only did the individual observations on this one day differ significantly from the three curves, $\chi^2=41.01$, $n=14$, but the three curves differed significantly from each other, $\chi^2=17.94$, $n=4$. The factors causing heterogeneity within series on this day presumably were operative between series as well, suggesting that the two curves with excessive χ^2's did not represent chance heterogeneity which would demand their inclusion with the remaining data. Though heterogeneous in composition and differing significantly from each other, the average curve for the two discrepant series agreed satisfactorily with that computed from the remaining data, as is shown graphically by the distribution of the crosses about the curves in Figures 1 and 2. In the absence of any systematic difference, most of the later calculations have been restricted to the 19 series with a known internal homogeneity.

Other workers on dosage-effect relations have reported agreement of the order observed here between the individual lots of eggs in a single series and their respective curves, but it is rare that this homogeneity carries over into the relation between individual curves. The equivalence of the separate curves has been tested by computing χ^2 for the scatter of all individual observations about a single standard curve without regard to their subdivision into series, and then subtracting from this total χ^2 the sum of the χ^2's for the individual series. This remainder represented differences in both the position and slope of the individual curves but when required, the χ^2's for the variation in these two parameters have been determined separately.

The standard dosage-survival curve for roentgen rays upon *Drosophila* eggs, as determined from the data of all 21 series, had the equation

$$y=6.0639-3.8402x,$$

where y is the survival in probits and x is the log-dose of roentgen rays in roentgens /100. The variation of the individual observations about this line indicated a poorer agreement than that for most of the constituent series, with $\chi^2=217.30$, $n=189$ and $P=0.15$. When restricted to the 19 series known to be homogeneous, the standard curve agreed closely with that based upon all the data, having the equation

$$y=5.0487\pm0.0063-3.8164\pm0.0437\,(x-0.2649)$$

or

$$y=6.0597-3.8164x.$$

The smaller variation about this second line was reflected clearly in the test for homogeneity, with χ^2 less than the number

of degrees of freedom, $\chi^2 = 168.84$, $n = 175$. Under these experimental conditions the standard dosage-survival curve maintained a remarkable stability when determined from constituent series with a demonstrable internal consistency. The expected dose in roentgens for any given survival could be predicted from the above equation in 19 cases out of 20 with a precision varying from 0.7 per cent of the predicted dose at 50 per cent survival to 1.4 per cent of that at 20 or 80 per cent survival. The original graphic standard curve reported previously, $y = 6.1005 - 3.957x$, differed slightly, though significantly, from the computed estimate.

Although the individual observations agreed well with the standard curve, the variation between series has yet to be isolated. The total χ^2 of 168.84 with $n = 175$ includes the scatter of the original lots of eggs about their respective 19 curves, amounting to $\chi^2 = 115.38$ for $n = 139$. The differences, $\chi^2 = 168.84 - 115.38 = 53.46$ and $n = 175 - 139 = 36$, measures the variation of the individual curves from the standard curve in respect to both slope (b) and position (a), a χ^2 close to the 5 per cent level of significant disagreement.

The source of this near-significant discrepancy may be sought in several factors. More than seven years elapsed between the first and the last series, but no trends were evident during this period, either in slope or in position. The flies in the experiments came from three different stocks, originating in Oregon, in Florida and as an isogamic stock, but the mean curves for all three were substantially equivalent, the χ^2 for the divergence between them totalling 4.93 with $n = 4$. Comparing the component curves within each stock, those determined from both the Florida and the isogamic flies agreed very well with one another. The dosage-survival curves for the 11 homogeneous series from the Oregon stock, on the other hand, varied moderately in slope ($\chi_b^2 = 14.97$, $n = 10$) but significantly in position ($\chi_a^2 = 21.18$, $n = 10$). Of the two terms or parameters defining a dosage-survival curve, the slope b has usually shown a greater constancy than the position in studies of drugs and other toxic agents, just as in the present experiments on the Oregon stock. Usually, however, so few individuals are used at each dose that differences of the relatively small magnitudes observed here are concealed by the errors of sampling. With the present large numbers for each percentage, averaging 275 eggs, smaller shifts in susceptibility could be recognized.

SUMMARY AND CONCLUSIONS

A statistical examination of the dosage-survival curve for *Drosophila* eggs under roentgen irradiation as recorded by a standard technique in a single laboratory has shown that the standard curve has a greater stability in both slope and position than has been reported generally in investigations of toxic effects. Through the use of large numbers for each percentage, the sampling errors have been reduced sufficiently to test this stability critically. Two curves in the 21 forming the complete data lacked internal consistency by the χ^2 test and were omitted. Ignoring differences between curves, the mean slope and position for the remaining 19 series were well supported by the individual observations. However, a comparison of the component curves, which agreed with their respective observations rather better than would be expected on the average, indicated a heterogeneity between them approaching the 5 per cent level of significance. Closer examination traced this primarily to significant shifts in the over-all level of susceptibility within one group of curves. Investigations of other toxic agents have likewise shown a greater instability in the level of susceptibility than in the slope.

In working with roentgen-ray effects requiring a high degree of precision, a curve determined under standard conditions should parallel the experimental series to insure against small changes in susceptibility. Usually, however, if the standard curve for a particular laboratory and technique agrees well with the equation which

is given here for the mean curve, it is probably safe to use this equation for converting each observed percentage of hatched eggs, corrected for the fertility of the controls and transformed to a probit, directly to the log-dose in roentgens. In this case little is gained by increasing the number of eggs per lot beyond 100 or 150 if the mortality falls within a range of 10 to 90 per cent.

REFERENCES

1. BLISS, C. I. The determination of the dosage-mortality curve from small numbers. *Quart. J. Pharm. & Pharmacol.*, 1938, *11*, 192–216.
2. FISHER, R. A., and YATES, F. Statistical Tables for Biological, Agricultural and Medical Research. Oliver and Boyd, London, 1938, pp. 1–90.
3. PACKARD, CHARLES. The biologic measurement of depth doses. *Radiology*, 1937, *29*, 12–21.

Vol. 46, No. 3

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

Editor: Lawrence Reynolds, M.D. *Assistant Editor:* Ruth Bigelow, B.S.

Editorial Board: A. C. Christie, M.D. E. H. Skinner, M.D. Lauriston S. Taylor
Advisory Board for Pathology: James Ewing, M.D. Eugene L. Opie, M.D.
Collaborating Editors: The Officers and Committee Members of the Societies of which this Journal is the official organ, whose names appear on this page, are considered collaborating editors of this Journal. *Foreign Collaborators:* Gösta Forssell, M.D., Stockholm, G. F. Haenisch, M.D., Hamburg, R. Ledoux-Lebard, M.D., Paris.

Publisher: Charles C Thomas, 220 East Monroe St., Springfield, Illinois.

Issued Monthly. Subscription $10.00 per year, $11.00 in Canada and $12.00 in foreign countries. Advertising rates submitted on application: Editorial office, 110 Professional Building, Detroit, Mich., Office of publication 220 E. Monroe St., Springfield, Ill. Information of interest to all readers will be found on page iv.

Officers and Standing Committees

THE AMERICAN ROENTGEN RAY SOCIETY

President: M. C. Sosman, Boston, Mass.; *President-Elect:* W. M. Doughty, Cincinnati, Ohio; *1st Vice-President:* G. E. Richards, Toronto, Ont.; *2nd Vice-President:* J. C. Dickinson, Tampa, Florida; *Secretary:* C. B. Peirce, Royal Victoria Hospital, Montreal, Que.; *Treasurer:* J. B. Edwards, 144 Woodridge Place, Leonia, N. J.; *Historian:* Percy Brown, 475 Commonwealth Ave., Boston, Mass.

Executive Council: M. C. Sosman, W. M. Doughty, G. E. Richards, J. C. Dickinson, C. B. Peirce, J. B. Edwards, Lawrence Reynolds, H. J. Walton, P. A. Bishop, U. V. Portmann, E. L. Jenkinson, J. W. Pierson, L. C. Kinney, B. P. Widmann, R. C. Beeler, Chairman, 712 Hume-Mansur Bldg., Indianapolis, Ind.

Program Committee: R. C. Beeler, Indianapolis, Ind., P. A. Bishop, Philadelphia, Pa., C. B. Peirce, Montreal, Que., U. V. Portmann, Cleveland, Ohio, Lawrence Reynolds, Detroit, Mich., W. M. Doughty, Chairman, Cincinnati, Ohio.

Publication Committee: H. M. Weber, Rochester, Minn., E. P. Pendergrass, Philadelphia, Pa., U. V. Portmann, Chairman, Cleveland, Ohio.

Finance Committee: H. D. Kerr, Iowa City, Iowa, C. M. Richards, San Jose, Calif., H. J. Walton, Chairman, Baltimore, Md.

Committee on Scientific Exhibits: V. W. Archer, University, Va., S. W. Donaldson, Ann Arbor, Mich., P. A. Bishop, Chairman, Pennsylvania Hospital, Philadelphia, Pa.

Member, National Research Council: Ross Golden, New York City.

Editor: Lawrence Reynolds, 110 Professional Building, Detroit, Mich.

Assistant Editor: Ruth Bigelow, 110 Professional Building, Detroit, Mich.

Editorial Board: A. C. Christie, E. H. Skinner, Lauriston S. Taylor.

Advisory Board for Pathology: James Ewing, Eugene L. Opie.

Forty-second Annual Meeting: Netherland Plaza, Cincinnati, Ohio, Sept. 23–26, 1941.

THE AMERICAN RADIUM SOCIETY

President: Hayes E. Martin, New York, N. Y.; *President-Elect:* William E. Costolow, Los Angeles, Calif.; *1st Vice-President:* J. E. Gendreau, Montreal, P. Q.; *2nd Vice-President:* George C. Wilkins, Manchester, N. H.; *Secretary:* A. N. Arneson, 4952 Maryland Ave., St. Louis, Mo.; *Treasurer:* Charles L. Martin, 3501 Gaston Ave., Dallas, Tex.

Executive Committee: W. P. Healy, Chairman, New York, N. Y., L. A. Pomeroy, Cleveland, Ohio, F. W. O'Brien, Boston, Mass.

Program Committee: W. E. Costolow, Chairman, Los Angeles, Calif., G. T. Pack, New York, N. Y., P. A. Nelson, Chicago, Ill., E. T. Leddy, Rochester, Minn.

Publication Committee: E. H. Skinner, Chairman, Kansas City, Mo., Zoe A. Johnston, Pittsburgh, Pa., W. P. Bailey, Los Angeles, Calif.

Research and Standardization Committee: Edith H. Quimby, Chairman, New York, N. Y., J. L. Weatherwax, Philadelphia, Pa., W. S. MacComb, New York, N. Y.

Education and Publicity Committee: A. W. Oughterson, Chairman, New Haven, Conn., L. R. Cowan, Salt Lake City, Utah, J. F. Hynes, Wilmington, Del.

Janeway Lecture Committee: Douglas Quick, Chairman, New York, N. Y., E. H. Skinner, Kansas City, Mo., G. Failla, New York, N. Y., W. P. Healy, New York, N. Y., L. A. Pomeroy, Cleveland, Ohio, F. W. O'Brien, Boston, Mass.

Committee on Arrangements: J. E. Wirth, Chairman, Baltimore, Md., J. G. Spackman, Wilmington, Del., J. V. Blady, Philadelphia, Pa.

Representatives on American Board of Radiology: Douglas Quick, New York, N. Y., R. H. Stevens, Detroit, Mich., B. P. Widmann, Philadelphia, Pa.

Twenty-seventh Annual Meeting: Atlantic City, N. J., June 8–9, 1942.

EDITORIALS

CARCINOMA OF THE LARGE INTESTINE

THE literature is replete with reports on carcinoma of the large intestine, and during the last several years a great amount of material has accumulated on all phases of this subject. Recently Buirge,[1] in a report on carcinoma of the large intestine, in which he makes a review of 416 autopsy records, calls attention to certain interesting phases of this all important subject.

It occurred, and quite rightly so, to Buirge that it would be interesting to take a group of cases in which autopsy had been performed for study of the nature of the lesion at the time, making an effort to analyze the difficulties that hedge about clinical recognition of this disorder. The basis for his material was obtained on the patients that came to necropsy in the department of pathology at the University of Minnesota between January, 1910, and July, 1937, because of carcinoma of the large bowel. This material Buirge found represented a fair sample of the general population.

In his statistical analysis he discusses the incidence, the age and the site, but what is of particular interest is an important subhead which he labels "problem of delay in diagnosis and treatment." If cancers, and particularly cancers of the intestine, are to be cured the patients must present themselves at a time when cure is possible, and to reduce the delay before treatment is of great importance in reducing the mortality from the disease. Buirge quite aptly says that the responsibility for this initial delay lies with the patient, but of equal importance are a correct diagnosis and early institution of adequate therapy on the part of the first physician that the patient consults. It is unfortunate that some of the delays encountered are due to the inability of the physician to make a correct and early diagnosis of cancer, even of cancer in more accessible parts of the body such as carcinoma of the breast and of the uterine cervix and of the lower part of the rectum as well as in the oral cavity. But for the physician to make an early diagnosis of carcinoma of the intestine requires considerable knowledge not only of the presenting symptoms in these cases but of the most probable site of the cancer in relation to the presenting symptoms.

Rankin, in 1933, in an analysis of a group of his cases, found that the average patient is conscious of some of the characteristic symptoms of cancer of the colon at least eleven months prior to seeking medical advice. Pack and Gallo in an analysis of 1,000 cases of cancer concluded that delay in treatment of the cancer was due to the patient alone in about 44.3 per cent, to the patient and physician in 18 per cent and to the physician alone in 17 per cent. These observers also came to the conclusion that a delay of three months or over from the discovery of symptoms to a visit to the physician was regarded as undue delay.

Numerous authors have called attention to the difficulties of differential diagnosis in the case of carcinoma of the intestine. Not only does a confusing clinical picture arise as a result of the location of the tumor but also as regards its rate of growth, its progressive nature and secondary systemic conditions which also occur within this age group.

A whole host of erroneous diagnoses often tend to delay the arrival at a correct diagnosis. It is interesting to note that Buirge

[1] Buirge, R. E. Carcinoma of the large intestine. *Arch. Surg.*, May, 1941, *42*, 801–818.

found that 16.6 per cent of the incorrectly diagnosed cecal lesions were diagnosed as appendicitis, while 8.3 per cent were diagnosed as cholecystitis. It is of great importance to note the fact that in this group of cases 5.2 per cent had had recent hemorrhoidectomies performed without discovering the primary lesion in the sigmoid or in the rectum.

Anemia was diagnosed in 10 instances without a knowledge of the precipitating cause of the anemia, this in spite of the fact that many observers have called attention to the importance of secondary anemia in cases of cancer of the colon; particularly proximal colonic lesions may simulate pernicious anemia.

The average duration of symptoms before diagnosis in this group of cases of carcinoma of the intestine was found to be thirteen months for lesions in the right side of the colon; twelve and a half months for lesions in the transverse and descending colon, and fourteen months for lesions in the sigmoid flexure.

It is a well known fact that early symptoms of carcinoma of the large intestine may be of such a vague and relatively insignificant nature that both the patient and the physician may be misled and such was true of 31 per cent of the incorrect diagnoses in this group of cases.

In this series 97 roentgen studies of the colon were reported in the autopsy records and in these the diagnosis in 84.5 per cent were correct; in 5.2 per cent they were uncertain and in 10.3 per cent they were incorrect. Buirge emphasizes that in this connection it should be mentioned that the progressive nature of the lesion necessarily indicates the repeated use of roentgen examination at intervals in keeping with the clinical progress of the disease. In the case of patients presenting themselves for gastrointestinal studies, the roentgenologist should keep in mind this injunction and if the immediate study is negative for evidences of a colonic lesion checkup studies within a few days should be suggested. Meticulous care should be exercised in the examination of the colon if operable lesions are not to be missed. Too frequently the roentgenologist bases his conclusions upon a study which has been made on a patient with inadequate preparation and where the detail and care in the study have not been sufficient. Since reliable clinical proof of early colonic cancer depends on the roentgenologic studies, this all important part of the examination cannot be lightly passed over.

THE USE OF IODIZED OIL IN ROENTGENOGRAPHY

THE use of iodized oils as a diagnostic aid in roentgenographic procedures has become so universal and commonplace that the history of their introduction into roentgenography is somewhat beclouded or neglected. Elsewhere in this issue of the JOURNAL will be found an article by Hartgraves on iodized oil in roentgenography, with animal experimentation, and it is of interest to note that the first experimenters in the use of iodized oil in roentgenography study were three American investigators, namely, Waters, Bayne-Jones and Rowntree,[1] who in 1917 carried out a series of experiments on living animals with the intention of acquiring a clearer conception of the anatomy and physiology of the lungs.

Their preliminary experiments were based on the previous therapeutic use of relatively large intratracheal injections and it occurred to them that a method might be devised whereby the air passages could be filled or coated with material opaque to the roentgen rays. The material which they used in their experiments was an iodoform preparation, iodoform having previously been used in the local treatment of pulmonary tuberculosis, in bronchiectasis, and in putrid bronchitis. From their preliminary work it was soon shown that a suspension of iodoform in olive oil in thin

[1] Waters, C. A., Bayne-Jones, S., and Rowntree, L. G. Roentgenography of the lungs; roentgenographic studies in living animals after intratracheal injection of iodoform emulsion. *Arch. Int. Med.*, 1917, *19*, 538–549.

layers definitely impeded the roentgen rays. As a result of investigation it was found that the most satisfactory material at that time was a 10 per cent suspension of iodoform in olive oil.

It is also interesting to note that in their animal experimentations a solution of thorium, which had recently been described by Burns as a valuable agent in pyelography, was used, but the shadows cast by this latter material were too faint and diffuse for practical value and the thorium was found to be more toxic than the iodoform emulsion.

A number of intratracheal injections of the iodoform solution was done and they came to the conclusion that this method was an excellent one, at least in animals, to delineate the air passages of the lungs, and from these preliminary studies the authors believed "that by such a method it may become possible to define with precision many radiographic shadows which are at present largely data for speculation."

It is unfortunate that this splendid experimental work should have been interrupted by the first World War in 1917 and that the passage of years has somewhat obscured this fundamental information which was obtained by Waters, Bayne-Jones and Rowntree.

It remained for two Frenchman, Forestier and Sicard, five years later, again to call the scientific world's attention to the possibility of the use of radiopaque oils in roentgenographic studies. By such a technique many obscure conditions of the lungs have been elucidated and it is of untold value as a diagnostic procedure.

The article by Hartgraves is a timely one for he not only aptly calls our attention to the historical development of the halogenated oils in roentgenography but he also points out some of their varied uses and from his own experimentation has helped to clear up some of the obscure points in the use of iodized oils, particularly in hysterosalpingography.

CLAUDIUS REGAUD
1870–1940

IN MEMORIAM*

CLAUDE REGAUD is no longer with us! He died at the end of December, 1940, following a lengthy and heroically borne illness, at his home at Couzon-au-Mont-d'Or near Lyon, where he had withdrawn because of his ailment. Deeply shocked at the news are not only those who have had the advantage of being associated with him as a man and as a scholar,

* From *Acta radiologica*, 1941, *22*, 327–330. Translated from the German through the kindness of Dr. James T. Case. The photograph accompanying the obituary is original and is from the collection of Dr. Case.—Ed.

but also all those who have regarded his life as a pattern for their own.

Claude Regaud belonged, in his development, to the Lyon School,[1] and it was also in Lyon that his fruitful career began. He had a particular interest for the study of histology, and his abilities, both as an inspiring scientist and as an organizer, procured for him in very short time a high regard in the laboratory of J. Renaut. During his incumbency at this institute, he was the author of outstanding works in the field of histology. In his researches his greatest care was to conduct his studies in a well-planned manner and to attack all problems from the ground up; his studies on the lymph vessels and on spermogenesis and ovogenesis are exemplary. He likewise turned his attention to technical problems and he was one of the first in France to devote himself to the study of the biological effects of irradiations on the tissues. By these studies, his development as a scientist acquired a new direction. The detailed investigations with which Regaud busied himself, and which he began in 1905, were chiefly concerned with the study of the testicle and the ovary of the higher mammalia. This work attracted the attention of Emile Roux, the Director of the Pasteur Institute, and induced him in 1911 to propose to Regaud that he come to Paris to build up a biological institute for the study of irradiations in affiliation with the physics institute, to be entrusted to Madame Pierre Curie. This was the origin of the Radium Institute of the University of Paris. The World War of 1914–1918 hindered the development of this Institute. Significant donations immediately following the War permitted the building to be begun anew. Regaud, who was occupying a teaching chair at the Pasteur Institute, had at his disposal in the beginning a department of the Hospital Pasteur, and later, in collaboration with his associates, founded the Fondation Curie, where, during the last twenty years, physicians and scholars from all over the world came together. Later he instituted the construction of a clinic in the immediate environs of the Fondation Curie, establishing a scientific center of first rank, whose chief task was the campaign against cancer.

Regaud had a natural inclination for teaching and followed this profession while still in Lyon, and afterwards at the Pasteur Institute. His teaching was characterized by a particular clarity, his lectures were well prepared, extremely precise, and easily understood.

His teachings and the changes which he made in time in the methods of irradiation, which he himself had built up, were opposed by some; those, however, who saw him at work, recognized the difficulties of the problems which he sought to clarify. The experiences which he acquired at the sick bed and from his experimental investigations were his guide. His task was the more difficult in that the proper evaluation of results frequently demanded the lapse of several years and rendered indispensable an exactly planned method of procedure.

Regaud and his school exerted an enormous influence on cancer research. His manner of thinking and of working was endowed with a widely disseminative power and it was not necessary to be his immediate collaborator in order to be influenced by his teachings. Regaud and his collaborators have been the authors of numerous works. Truly masterpieces among these are the *Archives de l'Institut du Radium de l'Université de Paris et de la Fondation Curie*, a series of studies devoted to radiophysiology and radiotherapy (roentgen, and Becquerel-Curie radiations), in which the discussions concerned with general and fundamental concepts and practical observations have been woven together in a harmonious manner. The *Index analyticus cancerologiae* is likewise, in its conception, a valuable document.

Regaud was not less occupied, in connection with cancer research, with the social problems, and he dedicated himself to this

[1] For the information as to details of Regaud's career we are indebted to Professor Policard of Lyon and it is therefore our duty to express here our warmest thanks for his kind compliance with our request.

task with exemplary unselfishness. With everything else he possessed a distinct talent for organization. Foreign governments and numerous institutions of both hemispheres turned to him for counsel and he undertook extensive travels and participated personally with all the vigor he possessed in the execution of the campaigns against cancer, not only in France itself, but also in various transoceanic regions.*

This posthumous biographical sketch would be incomplete if it concerned itself solely with the scholar and the organizer. Regaud the man primarily deserves the highest regard. The character of Regaud was unimpeachable, his uprightness was without flaw; every impulse of egotistical pride was foreign to him and, although he accepted distinctions (among other honors he was a member of the Académie de Médicine and Commandeur de la Légion d'Honneur), he did not seek them. He was a firm Catholic, and filled with an ardent Christian belief; his love of neighbor knew no bounds, and in the choice of his scientific collaborators, he exhibited a far-sightedness and an impartiality which was beyond all praise.

In his earlier years, Regaud had been an ardent mountain climber. He loved Switzerland and was filled with an admiring wonderment for our institutions and institutes of higher learning. Many of us were on terms of intimate friendship with him, and not less numerous were those of our circles who were his students and partisans. In the year 1930 he was the guest of the "Schweizerischen Röntgen-Gesellschaft."

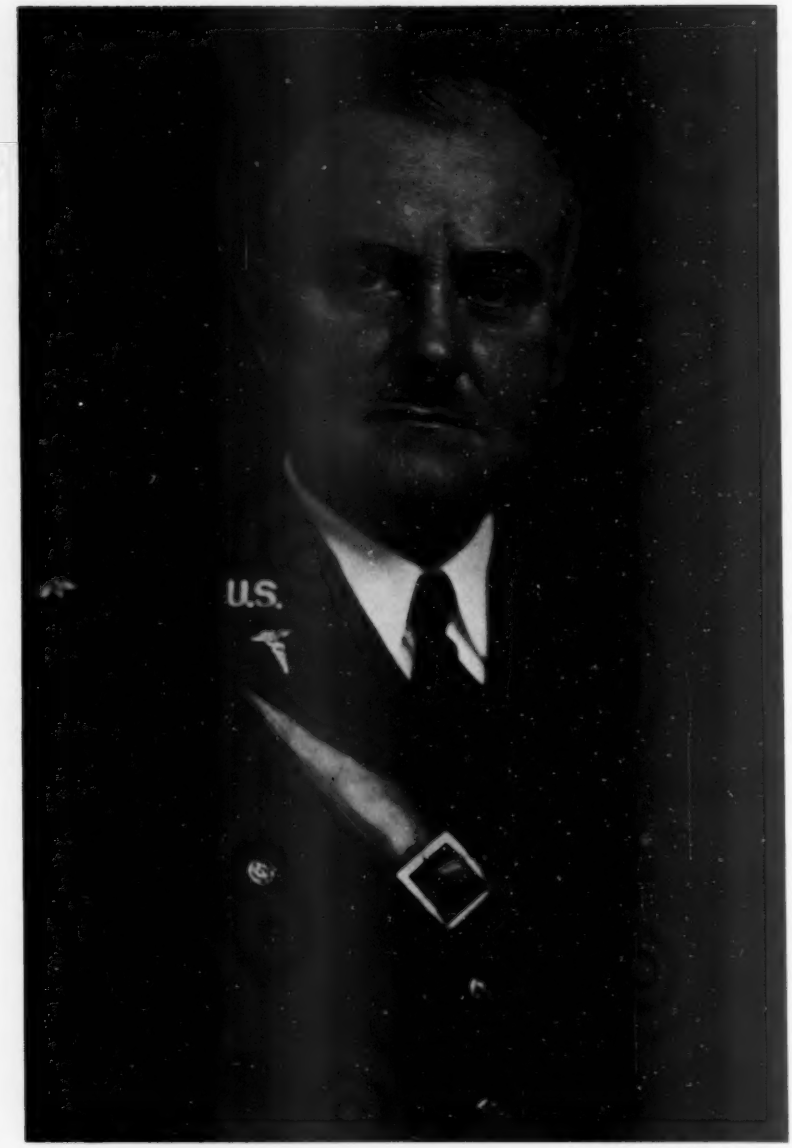
Following a life rich in accomplishments, devoted entirely to work and to scientific investigation, the last years of his life were clouded with misfortune and sorrows; doomed by a pitiless physical ailment, the mind of Regaud shared the despair of the misfortunes from which his native land has suffered, and in addition he lost a son, who died the death of a hero for his native country.

We bow in honor before Claude Regaud as a man, before his life of fruitful accomplishments, before his creative powers! His memory dwells in us inextinguishable, and his life and works will remain as a bright example for the living.*

René Gilbert

* The members of the American Radium Society will recall that at their annual meeting in 1924, during the presidency of Dr. James T. Case, Regaud was a guest of the Society and delivered a lecture on "Some Biological Aspects of the Radiation Therapy of Cancer."—Ed.

* A footnote states that this obituary was published in French in *Radiologia Clinica* and was reprinted in *Acta radiologica* in German with the permission of the author and the editors. —Ed.



U. S. Army Medical Museum

CHARLES A. STAMMEL
1886–1941

SINCE 1921, Lieutenant Colonel Charles A. Stammel has been one of the Army's most enthusiastic radiologists. His career was brought to a close by his sudden death at Fort Lewis, Washington, on May 25, 1941. This is sad news to his many friends who have appreciated and respected Colonel Stammel as a jovial friend and a kindly cooperative physician.

Colonel Stammel was born at Cincinnati, Ohio, on February 4, 1886. He was educated in that city, receiving his medical degree at the University of Cincinnati in 1910. He began service with the United States

Army by way of active duty with the Ohio National Guard in 1917. In 1918, after a course at the Army Medical School, he was appointed First Lieutenant, Medical Corps, regular Army. During the years of World War I he served at Camp Sherman, Ohio, LeMons, France and Vollander, Germany. Following the Armistice, he served at Brest, France, until 1920 when he was returned to the United States. Subsequent tours included duty at Fort Sheridan, Illinois, the Army Medical School, Washington, D. C., the Medical Field Service School in Carlisle, Pennsylvania and the Army and Navy General Hospital, in Hot Springs, Arkansas. In 1921, he received special training in roentgenology at the Army Medical School, and since that time his assignments have been mainly for roentgenological activities. These have included tours at Fort Sam Houston, Texas, William Beaumont General Hospital, El Paso, Texas, Philippine Islands, General Dispensary, U. S. Army, Washington, D. C., Fort Benning, Georgia, and Fort Lewis, Washington.

Colonel Stammel has contributed a number of roentgenological articles to the literature. He always recognized the unusual and he did not spare his energies to obtain pertinent details relative to such cases. Thereafter, he seemed to enjoy sharing his findings with his confrères. His professional attitude was one of scientific enthusiasm.

He was a member of the American Roentgen Ray Society, the Radiological Society of North America, an associate fellow of the American College of Radiology, a diplomate of the American Board of Radiology, a member of the American Medical Association and a fellow of the Association of Military Surgeons.

A. A. de Lorimier

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. C. B. Peirce, Royal Victoria Hospital, Montreal, Canada. Annual Meeting: Cincinnati, Ohio, Sept. 23–26, 1941.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Mac F. Cahal, 540 N. Michigan Ave., Chicago, Ill. Annual meeting: Atlantic City, N. J., June 10, 1942.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting: Atlantic City, N. J., June 8–12, 1942.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Fairmont Hotel, San Francisco, Calif., Nov. 30–Dec. 5, 1941.

RADIOLOGICAL SECTION, BALTIMORE MEDICAL SOCIETY
Secretary, Dr. Walter L. Kilby, Baltimore. Meets third Tuesday each month, September to May.

SECTION ON RADIOLOGY, CALIFORNIA MEDICAL ASSOCIATION
Secretary, Dr. J. D. Coate, 434 Thirtieth St., Oakland, Calif.

RADIOLOGICAL SECTION, CONNECTICUT MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets bi-monthly on second Thursday, at place selected by Secretary. Annual meeting in May.

SECTION ON RADIOLOGY, ILLINOIS STATE MEDICAL SOCIETY
Secretary, Dr. H. W. Ackemann, 321 W. State St., Rockford, Ill.

RADIOLOGICAL SECTION, LOS ANGELES CO. MED. SOC.
Secretary, Dr. Wilbur Bailey, 2007 Wilshire Blvd., Los Angeles, Calif. Meets on second Wednesday of each month at County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. Leo Harrington, 880 Ocean Ave., Brooklyn, N. Y. Meets monthly on fourth Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary, Dr. Joseph S. Gian-Francheschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. C. J. Challenger, 3117 Logan Blvd. Meets second Thursday of each month October to April inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati, Ohio. Meets third Tuesday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, J. O. Newton, 13921 Terrace Rd., East Cleveland. Meets at 6:30 P.M. at Midday Club on fourth Monday each month, October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. P. R. Weeks, 520 Republic Bldg., Denver, Colo. Meets third Friday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne County Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. J. N. Moore, 210 Professional Bldg., Ocala, Florida. Meetings in May and November.

GEORGIA RADIOLOGICAL SOCIETY
Secretary, Dr. R. C. Pendergrass, Prather Clinic Bldg., Americus, Ga. Meets in November and at annual meeting of Medical Association of Georgia in the spring.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Wm. DeHollander, St. John's Hospital, Springfield, Ill. Meets three times a year.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. H. C. Ochsner, Methodist Hospital, Indianapolis. Meeting held the second Sunday in May annually.

KENTUCKY RADIOLOGICAL SOCIETY
Secretary, Dr. W. C. Martin, 321 W. Broadway, Louisville. Meets annually in Louisville on first Saturday in April.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. Marcus Wiener, 1430-48th St., Brooklyn, N. Y. Meets Kings County Med. Soc. Bldg. monthly on fourth Thursday, October to May, 8:30 P.M.

LOUISIANA RADIOLOGICAL SOCIETY
Secretary, Dr. J. R. Anderson, 1130 Louisiana Ave., Shreveport. Meets annually during Louisiana State Medical Society meeting. Next meeting New Orleans, April, 1942.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. J. E. Lofstrom, 1536 David Whitney Bldg., Detroit. Three meetings a year, Fall, Winter, Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. I. I. Cowan, Mt. Sinai Hospital, Milwaukee, Wis. Meets monthly on first Friday at University Club.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. J. P. Medelman, 572 Lowry Medical Arts Bldg., St. Paul.

NEBRASKA RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday of each month, at 6 P.M. at either Omaha or Lincoln.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. A. O. Hampton, Massachusetts General Hospital, Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. H. J. Perlberg, 921 Bergen Ave., Jersey City. Meets annually at time and place of State Medical Society. Mid-year meetings at place chosen by president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. E. J. Ryan, St. Luke's Hospital, New York City. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse. Three meetings a year. January, May, November.

OHIO RADIOLOGICAL SOCIETY
Secretary, Dr. J. E. McCarthy, 707 Race St., Cincinnati. Meets at time and place of annual meeting of Ohio State Medical Association.

PACIFIC ROENTGEN SOCIETY
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, 416 Pine St., Williamsport.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

PITTSBURGH ROENTGEN SOCIETY
Secretary, Dr. H. W. Jacox, 4800 Friendship Ave. Meets second Wednesday each month, 4:30 P.M., October to June, Pittsburgh Academy of Medicine.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. S. C. Davidson, 277 Alexander St. Meets on second Thursday from October to May, inclusive. 8 P.M., Rochester Academy of Medicine Building.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Rocky Mountain Radiological Society
Secretary, Dr. A. M. Popma, 220 N. First St., Boise, Idaho. Annual meeting in Denver, summer of 1942.

St. Louis Society of Radiologists
Secretary, Dr. W. K. Mueller, University Club Bldg. Meets fourth Wednesday of October, January, March and May, at a place designated by the president.

San Francisco Radiological Society
Secretary, Dr. H. A. Hill, 450 Sutter St., San Francisco. Meets monthly on third Thursday at 7:45 P.M., first six months at Toland Hall, second at Lane Hall.

South Carolina X-Ray Society
Secretary, Dr. T. A. Pitts, Baptist Hospital, Columbia, S. C. Meets in Charleston on first Thursday in November, also at the time and place of South Carolina State Medical Association.

Tennessee Radiological Society
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg., Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. L. W. Baird, Scott and White Hospital, Temple, Texas.

University of Michigan Department of Roentgenology Staff Meeting
Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Radiological Society
Secretary, Dr. C. H. Peterson, 603 Medical Arts Bldg., Roanoke, Va. Meets annually in October.

Washington State Radiological Society
Secretary, Dr. K. J. Holtz, American Bank Bldg., Seattle. Meets fourth Monday each month, College Club, Seattle.

X-Ray Study Club of San Francisco
Secretary, Dr. J. M. Robinson, University of California Hospital. Meets monthly in evening on third Thursday.

Cuba

Sociedad de Radiología y Fisioterapia de Cuba
President, Dr. J. Manuel Viamonte, Hospital Mercedes, Habana, Cuba. Meets monthly in Habana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets monthly on third Thursday from November to June inclusive, at 8:15 P.M., 32 Welbeck St., London.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Faculty of Radiologists
Secretary, Dr. M. H. Jupe, 32 Welbeck St., London, W. 1, England.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to November inclusive.

Canadian Association of Radiologists
Secretary, Dr. A. C. Singleton, Medical Arts Bldg. Toronto, 5, Ontario.

Section of Radiology, Canadian Medical Association
Secretary, Dr. C. M. Jones, Inglis St., Ext., Halifax, N.S.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. Colin Anderson, Invercargill, New Zealand. Meets annually.

Continental Europe

Sociedad Espanola de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7. Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Saine, Paris

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel. Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aertze.
Permanent Secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the spring, and one in the fall.

Societa Italiana Radiologia Medica
Secretary, Prof. M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania. Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson. Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin. Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky. Meets monthly, first Monday, 8 P.M.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen. Meets second Wednesday each month October to July in Copenhagen, at 8 o'clock in State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6:30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University. Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto, Japan. Meets bi-monthly on third Sunday.

BULLETIN OF THE INTER-SOCIETY COMMITTEE FOR RADIOLOGY

THE EMPLOYMENT OF PHYSICIANS BY HOSPITALS: SOME LEGAL ASPECTS

By MAC F. CAHAL

(*Continued*)

Fiscal Arrangements

To illustrate the different relationships created under different types of agreements between physicians and hospitals, specific mention may be made of the various types of fiscal arrangements existing between radiologists and hospitals.[19] We are interested in determining when a physician is an employee and when he is an independent contractor.

Among radiologists practicing their specialty in hospitals in this country, 36.4 per cent are on a straight salary basis.[20] Another 7.3 per cent are paid a salary by the hospital plus a percentage of gross collections or net profits. The great majority of radiologists serve in hospitals on a commission basis, 47.3 per cent receiving as compensation a percentage of the gross or net income. It is hardly debatable that the hospital is itself practicing medicine as principal in those cases where a portion of the *net* income goes to the hospital as profit. About 9 per cent of radiologists practicing in hospitals lease the roentgen department, paying the hospital a monthly rental therefor, or performing charity work in lieu of rent.

Thus there are at least three different types of legal relationships created by agreement between hospitals and radiologists: (1) The radiologist may be an employee who receives as compensation for his services a percentage of the gross or net collections, or he may receive a fixed salary or a salary plus percentage. We have seen that if he is an employee, he is an agent or a servant. (2) The hospital and the radiologist may be partners under a joint enterprise agreement providing for a division of profits either on a percentage or a flat sum plus a percentage basis. (3) A relationship of landlord and tenant may be created under which the radiologist leases certain premises and pays to the landlord a fixed rental or a rental measured by a percentage.

Under the law of agency, the physician is a servant of the hospital under the first or the second type of arrangement. The elements of agreement, appointment and acceptance, consideration (salary or commission) and mutuality, all factors in the creation of an agency relation, are present. The master has the power to select and discharge the servant.[21]

It is a generally accepted principle of the law that an employer to whose benefit an act inures, is estopped to deny that the actor was his agent. He cannot accept the fruits of the relationship and avoid the vicarious liability which the law fixes upon him.[22]

Whether or not the radiologist is a servant when he rents the space utilized is another question. One may be both a lessee and agent, but where the intent of the parties, as evidenced by the whole contract and surrounding circumstances, was to create a lease, it will be so regarded,[23] and the acts of the tenant will impose no liability on the landlord. It has been repeatedly recognized that whether the relationship is one of agency or independent contractor is determined by the facts of each particular case.[24]

[19] See *Manual of Desirable Standards for Hospital Radiological Departments*, Chicago, The American College of Radiology, (1939), p. 10. The Council on Medical Education and Hospitals of the American Medical Association requires that a hospital, to meet the essentials for registration, must not operate the department of radiology as a source of profit. (Sec. 5, Par. 3.)

[20] Economics of the practice of radiology. *J. Am. M. Ass.*, 1939, *113*, 943-948.

[21] 18 R. C. L. 782.

[22] Mayor v Dean, 115 N. Y. 556, 22 N. E. 261, 5 L. R. A. 540. See Mechem, Floyd R. *Outlines of Agency*, Chicago, Callaghan & Company, 1923, Sec. 148.

[23] Oriental Investment Co. v Barclay, 64 S. W. 80; State v Page, 40 Am. D. 608; Colcord v Hall, 3 Heat (Tenn.) 625. 4 L. R. A. (N. S.) 698.

[24] Best Mfg. Co. v Peoria Creamery Company, 138 N. E. 684, 307 (Ill.) 238.

Tort Liability

Obviously, the courts have been convinced that employment of physicians by hospitals created an agency in fact when holding hospitals liable for torts of such employed physicians.[25] They have simply applied the familiar maxim of agency—*respondeat superior. Agentes et consentientes pari poena plectentur.*[26] Before going further, we should dispose of one point. The mere fact that a corporation is found liable in tort for the acts of employed physicians does not mean that such employment is legal. A corporation cannot employ an agent to perform any act which is not authorized by its own charter or by the law.[27] A principal can delegate to another no greater power or authority than he, the principal, possesses. Authority can flow only from the principal to the agent, not from the agent to the principal.[28]

Although the contract of employment as between the principal and his agent might be unenforceable because of illegality, it may nevertheless create liability in favor of third persons against the principal.[29] An agency illegal in its inception may be ratified to create liability in the principal.[30] A principal can ratify an illegal agency,[31] and an acceptance of a fee by a physician's employer has been held to constitute ratification making the employer liable on the physician's contract of guaranty.[32] Likewise, false and fraudulent representations by the physician are imputable to his employer.[33] The fact that the law requires a certain standard of skill does not prevent the relationship of master and servant arising.[34]

[25] See 2 C. J. Sec. 1041, and cases cited there.

[26] 5 Coke 80.

[27] 7 R. C. L. 621.

[28] LaBelle v Hennepin County Bar Assn., 288 N. W. 788, 244 Pac. 1089. (Corporation composed solely of attorneys.)

[29] Mechem, *op. cit.*, Sec. 53.

[30] *Ibid.*, Sec. 123.

[31] 2 C. J. Sec. 56.

[32] Jurkins v Pratt, 158 N. Y.S., 676, 2 C. J. Sec. 56; Homan v Redick, 96 Neb. 299, 149, N. W. 782, L. R. A. 1915 C, 601; Bourland v McKnight, 79 Ark. 427, 96 S. W. 179, 4 L. R. A. (N. S.) 698.

[33] 129 A. L. R. 337.

[34] *Restatement*, *op. cit.*, Sec. 220.

The cases in point provide ample authority for the conclusion that an employed physician is the agent of his employer.[35] The New York case of Renouf v New York

[35] 21 R. C. L. 395. ("It is generally held that persons and hospitals that treat patients for hire, with the expectation and hope of securing therefrom gain and profit, are liable for negligence and malpractice on the part of physicians or nurses employed by them.")

Stanley v Schumpert, 117 La. 255, 41 So. 565; Broz v Omaha Maternity, etc., 96 Neb. 648, 148 N. W. 575; Aderhold v Bishop, 94 Okla. 203, 221 Pac. 752, 60 A. L. R. 137.

21 R. C. L. 396. ("Clearly a corporation or an individual employing a physician to act as its or his agent is liable for the malpractice of the physician, being held *on the ordinary principles of agency*, as for example, where a department store runs a dental office in connection with and as a part of its business. This would be true, *a fortiori*, where the corporation employing the practitioner was not legally qualified to do business in the state.")

Tompkins v Pac. Mut. L. Ins. Co. 53 W. Va. 479, 44 S. E. 439. Hannon v Siegel Cooper Co., 167 N. Y. 244, 60 N. E. 597; Mandeville v Courtright, 142 Feb. 97.

United Dentists, Inc. v Bryan, (Va.) 164 S. E. 554. (Where a corporation practicing dentistry was held liable for the malpractice of a dentist employee. No question was raised or discussion as to whether or not dentist employee was independent contractor.)

Jenkins v Charleston, etc. (W. Va.) 110 S. E. 560. ("A hospital conducted for private gain is liable to its patient for injuries sustained by him in consequence of incompetence or negligence of a physician treating him at its instance, under a contract binding it to furnish him proper treatment. . . . For two good reasons *the defense of injury by an independent contractor* could not be maintained. The roentgenologist was employed and paid by the defendant to perform work in discharge of its own contract and undertaking to diagnose and treat the injury. . . .")

Brown v La Societe Francaise 71 P. 516, 138 Cal. 475. (The court held that where a hospital agreed to receive plaintiff for treatment on payment of $50 for an operation and $3.00 a day for room and surgeon performing the operation was the surgeon-in-chief of the hospital, who was paid by it by the month, the surgeon was the servant of the hospital, and not an employee of the patient.)

Gosnell v Southern Ry. Co. (N. C.) 162 S. E. 569. ("In the complaint alleged in the instant case, it is not alleged that Doctor Hilland was an employee of the defendant, Biltmore Hospital, Inc., or treated the plaintiff as the agent of said defendant. In the absence of such allegations, the facts stated in the complaint are not sufficient to constitute a cause of action against the defendant, Biltmore Hospital, Inc.")

See also Penland v French Broad Hospital (N. C.) 154 S. E. 406, to the same effect.

Gilstrap v Osteopathic Sanatorium Co., 24 S. W. (2nd) 249, ("Appellant insists that there was no evidence upon which to submit to the jury the question of defendant's liability for the acts of Doctor McReynolds in treating plaintiff's husband; that he was not defendant's agent but was acting in his own behalf. In view of all the facts and circumstances in this case, we are satisfied that appellant's contention cannot be sustained. It is admitted . . . that the defendant corporation owned and operated a large sanitorium for the treatment of human ailments and afflictions, that it maintained a large staff of physicians . . . ; that Doctor McReynolds, in addition to a salary paid by defendant, was given his room and board in said sanitorium and that he lived there, and that he got the same pay for his services whether he treated 1 or 150 patients; that the solemnly declared purpose and object of the corporation, among other things, was to treat all human ailments and afflictions. . . . The only reasonable and proper inference that may be drawn is that the deceased understood and believed that he was entering defendant's sanitorium as its patient to be treated by its physicians and surgeons, and that when he entered the sanitorium as its patient the rela-

Central Railroad is especially interesting.[36] In appealing a decision against the railway company, holding it liable for injuries sustained by a nurse while caring for an employee of the company on the order of its surgeon, counsel for the insurance company contended that a nurse, like a physician, is engaged in an independent calling and that neither can become the servant of another. This argument, said the Supreme Court of New York is fallacious. "Ordinarily the relation of master and servant does not exist between a person engaged in the practice of a profession and a person who engages him for a limited purpose or transaction. There is no reason, however, why that relation cannot be created. Frequently, lawyers, doctors and other men of skill are employed at regular salaries for definite periods of time. Such a contract of employment creates the relation of master and servant. *Greenberg v Jerome H. Remick & Co., 230 (N. Y.) 70, 75, 129 N. E. 211.* The relation may be created by contract either express or implied. *Brown v St. Vincent's Hospital, 229 App. Div. 402, 226 N. Y. S. 317.* . . . Whether or not the relation exists may be tested by the right of the employer to control or direct the work of the employee, the payment of wages, and the right to hire and discharge."

This decision was strengthened by differentiation on appeal to the highest court in *State Industrial Board v N. Y. Cent. R. R. Co. (N. Y.) 173 N. E. 218.* The railroad company appealed from a decision affirming an award of compensation. Said the court, "A trained nurse called in by a railroad company on a special case is not in the service of, or a servant of, the company, within the meaning of the Workmen's Compensation Act. She is a professional person like a physician, employed to exercise her calling to the best of her ability according to her own direction, subject only to the general directions of the physician in charge." The court said that the rule rests on the fact that one who employs such a nurse to take care of an injured person undertakes, not to treat the employee through the agency of the nurse, but to procure a nurse for the special purpose for which her services are required. Although the nurse engaged for special duty was in a general sense employed by the railroad company, she was not its employee. "She occupied the position of an independent contractor following her own calling, rather than that of one in the service of the employer." There may be a different rule, the court said in its dicta, in the case of a nurse who places her time and service at the call

---

tion of physician and patient was created between him and the defendant.")

Brandt v Sweet Clinic (Wash.) 8 P. (2nd) 972. ("It is next contended that the appellant Sweet Clinic, being a corporation, cannot practice surgery; therefore it cannot be held to respond in damages for malpractice by one of its surgeons. . . . The contention is without merit. The Sweet Clinic is a corporation carrying on a medical and surgical business for profit, and is liable for malpractice of the operating surgeons who in the cases at bar were employees of the corporation.")

Richardson v Carbon Hill Coal Co., 6 Wash. 52, 32 P. 1012. ("If, on the other hand, the company was conducting a hospital with its own physician for the purpose of deriving profit therefrom, or if it contracted with the appellant to furnish him with the services of a competent physician, and to properly treat him in case of an injury, it would be liable for the negligence or want of skill of its physician in attending him.")

Moulton v Huckleberry, (Ore.) 46 Pac. (2nd) 589. ("A physician who recommends or sends another physician to a patient is not liable for injuries resulting from the latter's want of skill or care unless the recommended physician is in his employment, or is definitely his agent or partner, or unless due care is not exercised in making the recommendation or substitution. . . . It plainly follows that where one physician is in the employment and is definitely the agent of another physician then the employing physician is liable for the negligent treatment or malpractice of his employee.")

Skidmore v Oklahoma Hospital, 278 Pac. 334. (The Oklahoma Supreme Court, quoting with approval Tulsa Hospital Association v Juby, Okla. 243, 175 Pac. 519, declared that when patients are accepted for financial gain, the hospital receives them "under the implied obligation that it will exercise ordinary care and attention for their safety. The hospital is liable in damages to the patients for the negligence of nurses and other employees.")

Lincoln Park Coal & Brick Co. v Industrial Commission et al. (Ill.) 148 N. E. 79. ("A corporation must exercise due care in selecting its physician employee.")

Vaughan v Memorial Hospital, 130 S. E. 481. ("A hospital incorporated and conducted for private gain for the benefit of its stockholders, is liable in damages to its patients for negligence or misconduct of its officers and employees. . . . In its contract it stands upon the same basis as any other contractor, and as to employees and third persons it is subject to the same general rule, *respondeat superior*.")

[36] Matter of Renouf v N. Y. Cent. R. R. 229 App. Div. 58, 240 N. Y. S. 720. See also Hearns v Waterbury Hospital, 66 Conn. 98, 33 Atl. 604. (". . . substantial justice is best served by making a master responsible for the injuries caused by his servant acting in his service, when set to work by him to prosecute his private ends, with the expectation of deriving from that work private benefit."

of her employer without regard to special services. Clearly, the court in reaching this decision, differentiated between a factual situation where a professional person is employed at a permanent stipend, and where he was called in for a special service to be rendered a third person.

The cases holding that a physician is not the servant or agent of his employer, but is rather an independent contractor, are decidedly in the minority. "The decisions of which the rationale is that physicians and surgeons are not the servants of their employers are referrable to the conception that they are 'professional men' who are engaged in the understanding that they are to 'exercise their profession to the best of their ability according to their own directions; but in exercising it they are in no way under his (their) orders or bound to obey his (their) direction.' This theory as to the nature of their position necessarily implies that they are independent contractors —a designation which has sometimes been specifically applied to them."[37] It should be emphasized here that the fact of control of the servant's acts by the master is not the criterion as to whether an agency relation exists; the right of control is the determining factor.[38]

An interesting statement of the minority view is contained in a Louisiana case[39] in which the Court of Appeals recognized the relationship of master and servant between a hospital and an employed surgeon, but stated that this represents an exception to the doctrine of *respondeat superior*, and quoted with approval from *France, 15 Bandry-Lacantinerie (3rd) 617:* "Thus a master is not responsible for the damages caused by the one who is habitually his employee, when the latter, although still in the exercise of his functions in using the things belonging to his master, acts in the premises under the orders of the third party."

An Arkansas case[40] held that a radiologist employed by a group of physicians was not agent of these physicians. West Virginia, on the contrary, has ruled that a radiologist employed by a hospital is an agent and not an independent contractor.[41]

At this point it should be remarked that there is an essential difference in the circumstances of a case where the physician is an employee of the corporation which collects his fees and not infrequently realizes a sizeable profit therefrom, and of a case where the physician is merely a member of the staff appointed by the hospital and is not in any sense its employee. In a case of the latter type, it is obvious that the hospital undertakes to procure the physician to treat on his own responsibility, not on the responsibility of the hospital. It is patent that the physician is not acting for the hospital; there is no contract of employment between hospital and physician. The patient, not the hospital, is paying the physician (with the obvious exception of charity cases). The hospital has not selected the patient's physician, nor could it discharge him. The corporation is not benefiting from the activities of the physician in the sense that a middleman or an employer benefits from the activities of an employee.

[37] 19 A. L. R. 1183; Ark. Midland Ry. Co. v Pearson, 98 Ark. 399, 135 S. W. 917. ("A physician cannot be regarded as an agent or servant in the usual sense of the term, since he is not and necessarily cannot be directed in diagnosing of diseases and injuries and prescribing treatment therefor, his office being to exercise his best skill and judgment in such matters, without control by those by whom he is called or his fees are paid." This case was quoted by the dissenting justices in Chicago, Rock Island & Pacific Ry. Co. v Britt, Ark. 74 S. W. (2nd) 398 holding that a contract between a surgeon and a railway company created the relationship of master and servant, and the master became liable for torts committed by the servant in the course of his employment.) Norton v Hefner, 132 Ark. 18, 198 S. W. 97.

[38] Wolf v Sulik, 93 Conn. 431, 4 A.L. R. 356. (". . . the master's liability for the negligence of his servant extends far beyond his actual or possible control over the conduct of the servant.") *Restatement, op. cit.*, Sec. 251. Income Life Ins. Co. v Mitchell, 168 Tenn. 471, 79 S. W. (2nd) 572. See Mechem, *op cit.*, Sec. 508.

[39] Jordan v Touro Infirmary, 123 So. 726.

[40] Runyan v Goodrum, 147 Ark. 481. 228 S. W. 397. ("Whereas, as we have already shown, the x-ray specialist, or roentgenologist, like the physicians and surgeons, unless he expressly contracts to produce certain results, has the right to, and must at all times, act according to his independent judgment and discretion in the exercise of his skill and learning in the treatment of human diseases. . . . It inevitably follows under the doctrine of our own cases that the relation of master and servant cannot exist between physicians who are not x-ray specialists themselves and the x-ray specialist, or roentgenologist, whom they employ to assist them in the diagnosis and treatment of disease.")

[41] Jenkins v Charleston Gen. Hosp., *Supra*, Footnote 35.

To facts like these, an official statement by the Board of Trustees of the American Hospital Association may be correctly applied: "The performance of diagnostic and therapeutic procedures by staff members constitutes the practice of medicine *in* hospitals. It is not the practice of medicine *by* hospitals."[42] But, we submit, the same practice by employees of the hospital constitutes the practice of medicine *by* hospitals.

An opinion rendered by Justice Cardoza for the New York Court of Appeals has been the source of no little confusion on this point.[43] In that case the court said, "The relation between a hospital and its physicians is not that of master and servant. The hospital does not undertake to act through them, but merely to procure them to act upon their own responsibility." It is manifest that this reasoning is not applicable where the physician is a full-time employee for whose services the hospital corporation charges and by which it profits. To deny this is to deny the common rules of agency engrafted into our system of law.[44] In finding for the defendant hospital in the instant case, the court relied largely upon the theory granting exemption for tort liability to charitable institutions.[45] Referring to the Schloendorff decision in a later case, the New York Supreme Court said, "It would seem that the decision was not based entirely on the ground that an eminent surgeon was an independent contractor."[46]

While there are many cases on record holding hospitals liable for the negligence of staff members, whether employees or not, the hospital is generally not liable for the acts of those outside its employment. The majority of the cases follow the theory that a hospital is not liable under the doctrine of *respondeat superior* for torts of physicians and nurses who practice on the premises in the independent employ of patients.[47]

There is a line of cases holding that negligent acts of a nature beyond the control of a proprietary hospital do not render it liable as master unless it has negligently chosen the personnel. This is apparently on the independent contractor theory.[48] On the other hand, private hospitals for profit have usually been held subject to the same legal standards of liability as other business corporations, and hence liable under the doctrine of *respondeat superior*, however carefully its staff was selected.[49] Many of the defalcations giving rise to the alleged cause of action for which hospitals have been held liable are clearly professional and due to mistakes in medical judgment made by carefully selected physicians and surgeons who are employed to practice their profession according to their own direction.[50] Such vicarious liability could arise only through the doctrine of principal and agent.

To be continued.

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY

At the recent radiological conference held in Denver under the auspices of the Denver Radiological Club, there was formed the Rocky Mountain Radiological Society with forty-two charter members. Officers elected were Dr. Leonard G. Crosby, Denver, Colorado, *President* and Dr. Alfred M. Popma, Boise, Idaho, *Secretary*. The next annual meeting will be held in Denver during the summer of 1942.

[42] Cahal, M. F. What is the Issue? *Illinois M. J.*, October, 1938.
[43] Schloendorff v N. Y. Hosp. Soc., 211 N. Y. 125, 105 N. E. 92.
[44] Holmes, Oliver Wendell, *The Common Law*, Boston, Little, Brown & Co., 1936, p. 228.
[45] Post, Footnote 49.
[46] Mills v Soc. of N. Y. Hosp., 242 App. Div. 245, 274 N. Y. Supp. 233.
[47] Barfield v South Highlands Infirmary, 191 Ala. 533, 68 So. 30 (1915); Simons v No. Pac. Ry. 94 Mont. 365, 22 Pac. (2nd) 609 (1933); Gosnell v Sou. Ry. 202 N. C. 234, 162 S. E. 569 (1932); Holland v Eugene Hosp. 270 Pac. 784 (1928); Pikeville Methodist Hospital v Donahoo (Ky.) 299 S. W. 159. ("Surgeons on the staff of the hospital are not agents or employees of the hospital.")
[48] Daly's Astoria Sanitorium, 291 N. Y. Supp. 1006.
[49] See 48 Yale L. J. 81 and cases cited there. Mulliner v Evangelisher Diakonnissenverein, 144 (Minn.) 392, 175 N. W. 699 (1920).
[50] See 48 Yale L. J. 83.

KENTUCKY RADIOLOGICAL SOCIETY

A meeting of the Kentucky Radiological Society was held in April at which time the following officers were elected for the ensuing year: *President*, Dr. D. Y. Keith; *Vice-President*, Dr. H. C. Herrmann; *Secretary-Treasurer*, Dr. W. C. Martin. Meetings are held annually the first Saturday in April in Louisville, Kentucky.

BROOKLYN ROENTGEN RAY SOCIETY

At a recent meeting of the Brooklyn Roentgen Ray Society the following officers were elected for the coming year: *President*, Dr. George Cramp, Brooklyn; *Vice-President*, Dr. Louis J. Taormina, Brooklyn; *Secretary-Treasurer*, Dr. Leo Harrington, Brooklyn.

BOOK REVIEWS

Books sent for review are acknowledged under: Books Received. This must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers as space permits.

THE HEAD AND NECK IN ROENTGEN DIAGNOSIS. By Henry K. Pancoast, M.D., Late Professor of Radiology and Director of the Department of Radiology, University of Pennsylvania; Eugene P. Pendergrass, M.D., Profesor of Radiology and Director of the Department of Radiology, University of Pennsylvania; and J. Parsons Schaeffer, M.D., Ph.D., Professor of Anatomy, and Director of the Daniel Baugh Institute of Anatomy, Jefferson Medical College. Cloth. Price, $12.50. Pp. 976, with 1,251 illustrations. Springfield, Illinois: Charles C Thomas, 1940.

It is difficult for a reviewer to do justice to this altogether admirable book for it contains so much material that only reading it will give one an adequate conception of its worth. Nothing of importance has been omitted that deals with the gross or roentgen anatomy of the head and neck in health and disease. The close collaboration between radiologist and anatomist has been a happy one for nowhere is it more important to base one's roentgenologic, surgical or neurologic judgment on sound anatomic knowledge than when dealing with the structures that make up the head and neck. This liaison has been so perfectly accomplished that one can find no cleavage plane between the authors. The value of the book is greatly enhanced by the original anatomic drawings and photographs of anatomic sections. These are of excellent quality and reflect great credit on the publisher. Regardless of the size of his library no radiologist, otolaryngologist, neurosurgeon or neurologist can afford to be without this book. Many chapters are complete expositions of their subjects. The work is a classic and cannot be praised too highly.

H. DABNEY KERR

THE RÔLE OF THE LIVER IN SURGERY. By Frederick Fitzherbert Boyce, B.S., M.D., Diplomate of the American Board of Surgery; Fellow of the American College of Surgeons; Visiting Surgeon: Charity Hospital of Louisiana at New Orleans, French Hospital, Mercy Hospital, Hotel Dieu, Southern Baptist Hospital and Touro Infirmary. Cloth. Price, $5.00. Pp. 365, with 44 illustrations. Springfield, Illinois: Charles C Thomas, 1941.

This monograph, the recipient of the quinquennial Samuel D. Gross Prize for research in surgery by the Philadelphia Academy of Surgery for 1940, has been made available to the public through this publication, in accordance with the stipulations of the Samuel D. Gross Prize Award.

The Assyrians and Babylonians regarded the liver as the chief organ and as the essence of life, and modern science is doing much to substantiate this view. It is now known to be one of the cardinal centers of vital functions, especially those of metabolism. An infinite number of observations on the relation of the liver to abnormal function and pathology have come from the laboratory and the clinic, but we all realize that the final synthesis is yet to be made. Since we do not know completely the functions of the liver, no tests of liver function can be more than suggestive, and while we now realize that the liver may, and frequently does, show important abnormalities secondary to disease originating in other organs, our knowledge of it is still in the twilight zone.

The author's approach, as indicated by the title, is from the viewpoint of the surgeon, almost from the interest of the operator rather than from that of the diagnostician. The chapters discuss liver deaths and the hepatorenal syndrome, autolytic peritonitis—an experimental and clinical problem—the hepatic factor in thyroid disease, the hepatic factor in nonbiliary and non-hepatic disease, latent hepatic dysfunction and the "liver weakling," and the practical consideration of the hemorrhagic diathesis in jaundice. There are two chapters on tests of hepatic function, one on the usual tests and one on the Quick hippuric acid test. Another chapter is concerned with therapuetic considerations based on the liver factor in surgery. In an appendix, the physiology of the liver is clearly and completely summarized. The illustrations are pertinent and consist mainly of charts and beautifully reproduced photomicrographs. The approach to all sub-

jects is the historical one, and each section is well documented, with a full bibliography at the end of each chapter, together with additional references.

Since the liver behavior and function is so interrelated with disease and activity of other organs, and so much influenced by abnormalities of nutrition and the technique of operation, notably anesthesia, anyone doing more than casual surgery must have an interest in the subject matter of this book. The format is attractive, with excellent paper, and clear and readable type. The book is in fact a well-written presentation of our present-day knowledge of an important subject. It is in essence a readable summary of the literature on the relation of the liver to the everyday problems of the surgeon, and as such is recommended to surgeons, laboratory workers, and all others interested in the liver and its functions. Its defects are not those of the author, but of our still inadequate knowledge of the function of the liver in health and disease.

FREDERICK A. COLLER

DAS BRUSTBEIN UND SEINE GELENKE: Normale und krankhafte Befunde, dargestellt zum teil Mittels neuer röntgenologischer Methoden. (*Fortschr. a. d. Geb. d. Röntgenstrahlen*, Ergänzungsband 58.) Von Dr. E. A. Zimmer, Assistent am Röntgeninstitut der Universität Basel. Paper, price RM. 13; bound, RM. 15. Pp. 70, with 81 illustrations. Leipzig: Georg Thieme, 1939.

This study on the sternum and its joints is based on work carried out in the Roentgen Institute of the University of Basel. Diseases and disorders of the sternum and of the sternoclavicular joints are studied and illustrated by two new methods of roentgen examination. Both methods are based on a double exposure with the object of study close to the screen and the shadows of other parts obliterated by a shift in the position of the tube. The patient is instructed to breathe during the exposure and the tube is placed with the focal spot close to the surface (this requires a special type of shock proof equipment) of the patient's back. In the first method for the study of the sternum, the first exposure is made with the focal spot of the tube at the lateral chest wall, and the ray directed toward the sternum; and for the second exposure on the same screen, the tube is shifted to the opposite chest wall and downward one half on the intercostal space. The shadows of the ribs and spine are thus obliterated and the sternum appears in considerable detail. For the examination of the sternoclavicular joints the two exposures are made with the focal spot just above the level of the spinous process of the seventh cervical vertebra and 5 cm. to each side of the midline. The central ray of each exposure is directed parallel to the sagittal plane. The exposures are of the order of magnitude of 55 kv., 100 ma. and 0.1 second.

Studies on normal children show a great variation in the number and time of appearance of the ossification centers and also in the time of their fusion which covers a period of over ten years. The anatomy of the adult sternum is described in detail with variations in the size and shape of its parts. Included among the interesting anomalies are the presence of episternal bones seen in five women and one man, "angulus exostoses" at the sternomanubrial joint, foramina and fissures in the sternum and variations in the fusion of ossification centers. Sometimes there is a segmental shift so that the superior synchondrosis comes at the third rib rather than the second and there may be no superior synchondrosis at all. Variations in the formation of the first two ribs are called Srb's rib-sternum anomaly after an observer who gave a description in 1862.

Fractures of the sternum are best recognized in the lateral view. They are important principally because of the possible complications of mediastinitis and mediastinal hemorrhage. Dislocation at the sternal joints is very rare and in the majority of reported cases the manubrium is displaced anteriorly. Fractures and dislocations about the sternoclavicular joints are well visualized with the double exposure technique.

Among the general diseases affecting the sternum are rickets, multiple myeloma, von Recklinghausen's and Paget's diseases, and the changes are readily demonstable by the new techniques. Many local conditions in the sternum are also described and illustrated including tuberculosis, lymphogranulomatosis and neoplasm both primary and secondary. Mention is also made of luetic, actinomycotic and osteomyelitic involvement which has been described in the literature.

Arthrosis deformans rarely involves the sternoclavicular joints, but when it does the roentgen signs are narrowing of the joint space, sclerosis and flattening of the approximating surfaces and lipping. Degenerative changes involve the joints early and, according to Langen,

a normal joint is rarely seen as late as the fourth decade. Two cases of tuberculous sternoclavicular arthritis and one case of pyogenic arthritis are reported with illustrations. An aseptic necrosis of the clavicular head known as Friedrich's disease is described and a probable instance in a boy, aged seventeen, is reported. In observing the proximal end of the clavicle no pathological significance is to be attached to the notch sometimes seen on the inferior surface where the clavicle passes over the first rib. The double exposure technique is valuable for demonstration of a variety of pathologic lesions involving the sternal end of the clavicle.

A painful condition with overlying soft tissue swelling affecting the superior synchondrosis of the sternum called osteochondritis and perichondritis is presented with roentgenograms and microscopic sections. Xiphoiditis is usually an occupational disorder and may be very painful. It is analogous to coccygodynia and there are no changes demonstrable roentgenographically.

William A. Evans, Jr.

INDEX TO ABSTRACTS

ROENTGEN DIAGNOSIS

Neck and Chest

Canuyt, G., and Gunsett, A.: Sagittal planigraphy of the larynx 426
Potter, H. E.: Miniature films in chest survey 426
Saye, L., and Caubarrere, N.: Method of de Abreu in diagnosis of tuberculosis in large groups of individuals 427
Punch, A. L.: Diseases of the right middle lobe of the lung 427
Lynch, K. M., and Smith, W. A.: Pulmonary asbestosis 427
Charache, H.: Bronchogenic carcinoma with subcutaneous metastases 428
Munk, E.: Multiple disseminated pulmonary calcifications in mitral disease 428
Levi-Valensi, A.: "Chronic bronchitis of natives," manifestation of sclerotic pulmonary tuberculosis in former syphilitics ... 428
Debre, R., Lamy, M., Mignon, M., and Nick, J.: Roentgenologic study of infantile asthma 428
Jaubert de Beaujeu, A., Abdallah, T. B., and Picard, P.: Symmetrical pulmonary emphysema with multiple giant bullae 429
Sergent, E., and Kourilsky, R.: Pleural endothelioma 429
Sarmento Barata, J.: Cardiovascular roentgen kymography 429
Belbenoit, S., and Bonte, G.: Roentgenological appearance of pericardial traction 430
Delherm, L., Devois, A., and Rulliere (Mme.): Study of great vessels at the base of the heart by sectional roentgenography 430
Delherm, L., Devois, A., and Rulliere (Mme.): Study of great vessels at the base of the heart by sectional roentgenography 430

Abdomen

Singleton A. C.: Chronic gastric volvulus 430
MacCarty, W. C.: Cancer of the stomach 431
Hochmann, A.: Sarcoma of the stomach 431
Correia Neto, A.: Pyloric achalasia in the adult 432
Boon, T. H.: Intubation of small intestine 432
Gershon-Cohen, J., and Shay, H.: Ileocaecal tuberculosis 432
Rachet, J., and Arnous, J.: New roentgen method for study of the colon 433
Oury, P., and Peraly, E.: Gastric disorders associated with dolichocolon 433
Kleeberg, J.: Radiological diagnosis of tumors of the pancreas 433
Cashion, W. R.: Pericolic membranes 433
Saralegui, J. A.: Roentgenologic findings in exploration of the biliary tract 434

Genitourinary System

Macquet, P., and Lecoq, P.: Congenital stenosis of the ureter 434

Skeletal System

Jaubert de Beaujeu, A., and Benmussa: Congenital astragaloscaphoid synostosis, bilateral and isolated 435
Passebois, P., and Betoulieres, P.: Infantile vertebral osteochondritis 435
Passebois, P., and Betoulieres, P.: Roentgen picture of the notch in the vertebral body of the infant 435
Potozky, H., and Freid, J. R.: Ewing's tumor simulating sarcoma of soft-tissue origin 436
Weil, P. E., and Perles, S.: Clinical examination of bone lesions 436
Forestier, J., and Metzger, J.: Key to early diagnosis of spondylarthritis is in roentgenography of sacroiliac articulations 437
Weissenbach, R. J., and Lievre, J. A.: Osteitis fibrosa without parathyroid adenoma. 437

Blood and Lymph System

Baker, C., and Mann, W. N.: Hodgkin's disease 437

General

Jonscher, K.: Etiology and pathogenesis of the toxicoses in infants 438
Trostler, I. S.: Contributory negligence as it applies to medical malpractice 438

ROENTGEN AND RADIUM THERAPY

Deucher, W. G.: Restoration of normal activity of the patient as the object of irradiation in distant metastases 438
Levin, I.: Pathogenesis and radium therapy of mixed tumors of the salivary glands 439
Paterson, R., and Nuttall, J. R.: Evaluation of risk of biopsy in squamous carcinoma 440
Binkley, J. S.: Aspiration biopsy of tumors of the liver 440

COCCHI, U.: Short contribution to the question of leukoplakia, syphilis and malignant tumor 440
KOLBOW, H.: Decreasing the dose by the use of harder rays in roentgen diagnosis as shown by intravaginal measurements of dosage 441
GRYNKRAUT, B.: Therapeutic dose in treatment of malignant tumors 441
NØRGAARD, F.: Development of fibrosarcoma as a result of intra-articular injection of radium chloride for therapeutic purposes .. 442
LABORDE, S.: Dangers of radioactive substances introduced into the body 442
WOLF, K.: Vacuolar degeneration of carcinoma cells irradiated with roentgen rays .. 443
KASABACH, H. H., and MERRITT, K. K.: Capillary hemangioma with extensive purpura 443
SCHAEFER, F.: Close roentgen irradiation in blood vessel tumors—hemangiomas 444
HEEREN, J. G.: Roentgen irradiation combined with ultrashort wave irradiation and insulin treatment 445
ASH, J. E.: Epithelial tumors of the bladder ... 445
COLBY, F. H.: Supervoltage radiation in treatment of bladder tumors 445

ABSTRACTS OF ROENTGEN AND RADIUM LITERATURE

ROENTGEN DIAGNOSIS

NECK AND CHEST

CANUYT, G., and GUNSETT, A. Planigraphies de face du larynx. (Sagittal planigraphy of the larynx.) *J. de radiol. et d'électrol.*, May, 1939, *23*, 193–202.

The authors have published a series of articles on this subject, beginning with May, 1937. They regret the fact that other investigators have not followed their example. They have found the method exceedingly important in discovering lesions, either missed or unattainable by laryngotomy, in differential diagnosis, in determining the extent of the lesions especially from the operative point of view, and in checking the results of radiation therapy. The technique was as follows: 45 cm. distance, 75 to 80 kv., 150 ma., time 1.2 to 1.5 seconds; the focal spot is the Adam's apple. Sections are made at 1, 2, 3 and 4 cm. with those at 2 and 3 cm. found to be best. Exposures were made in various types of phonations; A, E, I, O, U; in apnea after inspiration; in apnea after expiration; in valsalva which produces distention of the ventricles, the vestibule and the pyriform sinus. Differences were also described in singing various notes.

Studies in all types of laryngeal affection are also demonstrated: (1) recurrent nerve paralysis; (2) polyp of the vocal cord; (3) small carcinoma of the vocal cord; (4) carcinoma of the aryepiglottic fold; (5) hemilaryngeal carcinoma; (6) hypopharyngeal carcinoma; (7) laryngopharyngeal carcinoma.—*M. L. Sussman.*

POTTER, HOLLIS E. Miniature films in chest survey. *Radiology*, Jan., 1940, *34*, 62–65.

Though the death rate from tuberculosis has been reduced in recent years it is still the commonest cause of death in persons from fifteen to forty-five years of age. Not over 5 per cent of the cases are diagnosed in the earliest stage when easily curable; 15 per cent are moderately advanced when diagnosed and 80 per cent far advanced. In order to find a high percentage of early cases it is necessary to examine not only sick people but those who are apparently well. Tuberculin tests have proved less reliable than roentgen examination in detecting such cases but the ordinary roentgen survey for tuberculosis is very expensive.

The author thinks this difficulty may be met by making miniatures from the fluoroscopic screen. The idea of making film miniatures by focusing down the image on a fluorescent screen is a very old one. The modern machine and tube give enough light but it has been hard to make a miniature of the size and detail required.

This has become possible now by the use of a fluorazure screen which gives off a brilliant blue-violet light with high actinic values. The film that is most sensitive to this blue-violet light is the ordinary commercial roentgen film. A lens was also found that was suitable for the

purpose. It was made originally for the purpose of night photography from airplanes. Several series of tests in making such miniature films are described. It remains only to try the method out in a practical field survey including thousands of cases. The author is very hopeful of the results.—*Audrey G. Morgan.*

Saye, L., and Caubarrere, N. La pratique de la méthode de de Abreu pour le diagnostic de la tuberculose dans les collectivités. (The method of de Abreu in the diagnosis of tuberculosis in large groups of individuals.) *Presse méd.*, March 25, 1939, *47*, 462–464.

The authors used the method of de Abreu in over one thousand subjects. They compared the results of roentgenoscopy, roentgen photography and ordinary roentgenography. The authors use a 10 kw. tube, a fluoroscopic screen 30×40 cm. (Siemanns Super-Astral), Leica camera with F 1.5 lens, tube screen distance 60 cm., focal distance 90 cm., film isochrome Agfa F 270. For school children 72 to 75 kw., 150 ma., 0.2 to 0.3 sec. For adults 80 to 90 kw., 180 ma., 0.3 to 0.5 sec. A diapositive was constructed which permitted the inclusion in each roentgen photograph of the name of the subject, date, etc. The authors are enthusiastic about the value of the method. They state that it has decided advantages over roentgenoscopy in the recognition of early lesions in children. They are still unprepared to state the limitations.—*M. L. Sussman.*

Punch, A. Lisle. Diseases of the right middle lobe of the lung. *Lancet*, Jan. 6, 1940, *1*, 5–7.

Detailed studies of the chest, including lateral and oblique projections, as well as the more elaborate procedures such as bronchography and tomography, have led to a greater degree of accuracy in the localization of pulmonary lesions. In particular, lesions of the right middle lobe can thereby be identified. Because of the frequency of such lesions, the author is describing with case examples, five types of involvement: pneumonia, bronchiectasis, massive collapse, bronchial carcinoma and interlobar effusion.

Atelectasis. When there is obstruction of the main bronchus concerned with the right middle lobe, collapse of it causes the lobe to recede from the anterior and lateral portions of the chest wall; compensatory emphysema of the upper lobe occurs to fill the space formerly occupied by the middle lobe so that displacement of the heart to the right does not result—as it does in case of collapse of the lower lobe. The middle lobe itself may appear as a small triangular area of increased tissue density, close to the right border of the heart. With lesser degrees of atelectasis, the size of this density is of course greater. Any evidence of atelectasis should serve to indicate need for bronchoscopy.

Lobar Pneumonia. The middle lobe is simply outlined by increased density without there being any significant contraction.

Bronchiectasis. Bronchiectasis is most often found in one or the other lower lobe but it may occur in the middle lobe and be confined to it. Three theories are cited to explain middle lobe involvement: (1) that it is a sequel to pneumonia, (2) that it is congenital—the bronchiectasis developing in portions of lung which did not expand at birth and (3) that it is a result of pressure on the bronchus by enlarged mediastinal glands.

Bronchial Carcinoma. Bronchial carcinoma is now known to occur relatively frequently. The neoplasm is usually located in a main bronchus, 1 to 2 inches beyond the bifurcation of the trachea, though it may be located in any branch including any of those in the middle lobe.

Interlobar Effusion. With a collection of fluid within the lesser fissure of the lung, there may be produced an opacity occupying the position of the middle lobe. Distinguishing criteria are not cited.—*A. A. de Lorimier.*

Lynch, Kenneth M., and Smith, W. Atmar. Pulmonary asbestosis. v. A report of bronchial carcinoma and epithelial metaplasia. *Am. J. Cancer*, August, 1939, *36*, 567–573.

Anderson and Dible studied the silica content of the lungs and the histologic evidence of pneumoconiosis in 70 persons who had died of pulmonary carcinoma and in 50 non-cancer subjects. A greater lung silica content was found among those with cancer than among the control series. Klotz reported an incidence of cancer to the extent of 8 per cent among 50 cases of asbestosis, though among 4,500 necropsies only 1.18 showed carcinoma.

A case of carcinoma coincident with asbestosis is described in detail. The authors emphasize the fact that they have noted 2 other cases of carcinoma among 35 cases of asbestosis—an incidence of approximately 6 per cent as com-

pared with an incidence of 0.3 per cent of carcinoma among 2,343 consecutive necropsies of other than asbestosis. Moreover they have noted in several cases of asbestosis a metaplasia of the bronchial mucosa of the sort which is likely to change into carcinoma.—*A. A. de Lorimier.*

CHARACHE, HERMAN. Bronchogenic carcinoma with subcutaneous metastases. *Am. J. Cancer*, Nov., 1939, *37*, 431–434.

Subcutaneous metastases in connection with bronchogenic carcinoma have seldom been reported (in only about 2.8 per cent of the cases). These extensions are very small, usually (0.5 to 1.0 cm. in diameter) and they may appear at a distance from the site of the primary lesion. Careful search should be made for them in all suspected cases of lung cancer for they provide a relatively easy excision of tissue for study and establishing a diagnosis.

The author's case differs from most because of the unusual size of the metastatic tumor in the chest and because of there being an additional tumor in the thigh. The patient was an Italian male, aged thirty-nine, admitted because of the growth in his anterior thorax. About four months previously he had been bothered with night sweats, weakness and loss of weight. At that time roentgen studies visualized a rounded density extending upward from the left hilus. A few months later he had noted a small nodule on his chest. This had grown rapidly during the month until it reached the size of a grapefruit. There then appeared the mass in his left thigh. Roentgen therapy was given and the superficial tumors receded but death occurred three months after admission and approximately seven months after the first appearance of symptoms. Autopsy revealed a bronchogenic carcinoma of the left upper lobe with extension into pulmonary arteries and veins, the left auricle, mediastinal and retroperitoneal nodes, the right ulna, the adrenals, pancreas, anterior chest wall and left thigh.—*A. A. de Lorimier.*

MUNK, E. Calcifications multiples disséminées dans les poumons dans la maladie mitrale. (Multiple disseminated pulmonary calcifications in mitral disease.) *J. de radiol. et d'électrol.*, Feb., 1939, *23*, 58–62.

A detailed report of a case is presented with autopsy findings. Mitral disease as a cause of pulmonary calcifications is somewhat unusual, ranking after tuberculosis, silicosis and echinococcus disease. The author reviews the numerous theories advanced to explain the mechanism of this process. He concludes that the pattern probably proceeds as follows: stasis, altered metabolism, focal necroses, and finally calcifications. Microscopically, the changes in the alveoli consist of fibrosis, destruction, amorphous granules in the interstitial tissues and degenerated alveolar cells, lack of vessels and osseous nodules.—*M. L. Sussman.*

LEVI-VALENSI, A. La "bronchite chronique des indigènes," manifestation de tuberculose pulmonaire scléreuse chez l'anciens syphilitique. ("Chronic bronchitis of natives," manifestation of sclerotic pulmonary tuberculosis in former syphilitics.) *Presse méd.*, March 25, 1939, *47*, 455–458.

A study of chronic bronchitis in the natives of North Africa indicated that a diffuse pulmonary sclerosis of an emphysematous type occurred with bronchial dilatation. The patients are in large part former syphilitics. The Koch bacillus is frequently the cause but is often difficult to demonstrate since it is a chronic process. There is experimental work to suggest that the pulmonary sclerosis with bronchial dilatation occurs as the result of the attenuated virulence of the bacillus and the tendency to fibrosis is particularly apt to occur in the presence of syphilis. Almost always there is a complicating cardiac insufficiency.—*M. L. Sussman.*

DEBRE, R., LAMY, M., MIGNON, M., and NICK, J. Etude radiologique de l'asthme infantile. (Roentgenologic study of infantile asthma.) *Presse méd.*, June 17, 1939, *47*, 957–960.

The changes found in asthma depend upon the size and shape of the thoracic cage, the position and appearance of the diaphragms, on the pulmonary hila and on the transparency of the parenchyma. The thoracic cage is usually enlarged at the time of an attack; the ribs become horizontal, the intercostal spaces are widened and the thorax becomes globular. Diminution in amplitude of the movement of the diaphragm is often marked. The diaphragm is lowered, flattened and descends towards the sinus. The left leaf separates itself to a considerable extent from the apex of the heart. The hilar shadow is abnormally widened, particularly vertically. It may extend from diaphragm to apex. The lungs give the impression of an acute emphysema during the attack followed by a diminution in

transparency due to the presence of a broncho-alveolar exudate. Most of the roentgen changes, apparent during a crisis, disappear in the interval.—*M. L. Sussman.*

Jaubert de Beaujeu, A., Abdallah, T. B., and Picard, P. Emphysème pulmonaire symétrique à bulles géantes multiple. (Symmetrical pulmonary emphysema with multiple giant bullae.) *Presse méd.*, March 12, 1940, *48*, 283–284.

The authors report a case of an adult about twenty-eight years of age who complained of small hemoptyses. His only past history was that of a slight cough for one and a half years which he attributed to bronchitis. There was a questionable family history of tuberculosis. Direct percussion of the superior thorax elicited a phenomenon of muscle edema, of a fullness and intensity which was unusual and was characterized by waves of extended and deep contractions. Auscultation was very instructive. In front and above, breath sounds were diminished bilaterally, somewhat more on the right than on the left. At the bases the breath sounds were normal but there were some râles. Behind, respiration was practically absent in the upper left chest. There were crepitant râles and rhonchi at both bases. Fluoroscopy gave the impression that half of the right thoracic cavity was empty. On the left the upper half was clear. The bases were normal. The hila were exaggerated. On the roentgenogram the appearance was the same on both sides, differing only in the size of the lesion. On both sides the dome of the thorax seemed empty, limited below by very fine lines which irregularly indicated the limit of the lung. On the right side the clear space occupied the upper half of the thorax, extending into adjacent lung. There were several straight or slightly concave lines which were superimposed on the lung. The hilar shadows were accentuated. In the lateral view the clear areas were superimposed upon one another occupying on the right side the entire thickness of the thorax.

In summary, the authors state that the most important sign in the diagnosis of multiple bullous emphysema is the presence of very fine lines between the homogeneous clear space and the adjacent lung tissue. Sometimes these fine concave lines are superimposed on the adjacent lung. Occasionally there is found reticulated tracks as described by Wiese, Heiken and Charr.—*M. L. Sussman.*

Sergent, Emile, and Kourilsky, R. Contribution à l'étude de l'endothéliome pleural. (Pleural endothelioma.) *Presse méd.*, Feb. 18, 1939, *47*, 257–259.

The authors report a case occurring in a man of sixty-two years of age. For twenty years he had been subject to paroxysmal cough lasting ten minutes. At the time of admission he noticed a tumefaction in the subclavicular region. A roentgen examination was said to be negative at this time. Three months later 350 cc. of a serofibrinous fluid was withdrawn from his chest. There was a rapid refilling of the pleural cavity. A diagnosis of neoplasm of the pleura was made and he was treated by radiotherapy. There were three possibilities for the origin of the tumor: (1) the bony thorax, (2) mediastinum, and (3) the lung. On clinical grounds these three sites were rejected and the diagnosis of a primary pleural tumor was made. The pleural fluid showed a large percentage of endothelial cells with nuclear disturbances and joined together by plasmodia. The patient was hospitalized with the idea of emptying the pleura of fluid by repeated aspirations to be followed by endoscopy. This was complicated by the very rapid reappearance of fluid. A number of spherical masses developed in the chest as seen roentgenographically, which simulated cysts because of their sharp round borders. These masses were situated anteriorly and were seen only when the chest had been emptied of fluid and thus could be revealed that these masses corresponded to endothelioma. Biopsy could not be performed because of the danger of hemorrhage.—*M. L. Sussman.*

Sarmento Barata, J. La radiokymographie cardiovasculaire. (Cardiovascular roentgen kymography.) *Presse méd.*, Feb. 18, 1939, *47*, 277–279.

The author uses a kymograph made of an aluminum disk, 18 cm. in radius on which are riveted lead triangles, apices toward the center, separated by 0.5 mm. The disc is driven on a central axis by an electric motor at a regulated uniform speed. The cassette is rotated on a second disk. The method is used for examination of valvular disorders, aortic and cardiac insufficiency, hypertension and cardiac function. However, it is of particular use in myocardial infarction in which the following observations can be made: (1) diminution or absence of pulsation; (2) systolic expansion.—*M. L. Sussman.*

BELBENOIT, S., and BONTE, G. Les images radiologiques de tiraillement péricardique. (The roentgenological appearance of pericardial traction.) *J. de radiol. et d'électrol.*, June, 1939, *23*, 248–262.

Observations are presented of 2 patients who developed severe cardiac syndromes after the installation of pneumothorax for tuberculosis. There was no previous history of cardiopathy. The findings were explainable on the basis of pericardial adhesions.

Roentgenologically these adhesions are found most often in tuberculous patients. The deformity that they produce may be accentuated or obliterated by pneumothorax. Two types of adhesions are described. The first is a mediastinopericardial spur whose site of predilection is along the left heart border and the costochondral junction. The deformity produced may vary with the phase of respiration. This is best seen by roentgenoscopy. The other is classified as an atypical deformity. It is usually produced by broad adhesions which are angular in shape and situated on either contour of the heart and also may be associated with the other type of band. Kymography aids in the differential diagnosis. When the appearance is diffuse, the bands are interpreted as being enveloped by a broad symphysis involving the pleural cavity. By contrast the mediastinal pericardial band is sharp and clean cut in appearance and the pleural cavity is free.

An anatomical study of these bands is presented. A significant point is that the pericardial cavity is not involved, the bands existing between the prepericardial tissue and the pleura.

Pathogenetically two factors are emphasized: the adhesion and the pulmonary retraction which puts tension on the adhesion. The clinical syndrome may be one of several types: (1) acute following pneumothorax in which a differential diagnosis must be made between embolus, mediastinal displacement and pleural reflex due to traction on adhesions; (2) subacute and chronic especially where no old cardiopathy exists; (3) anginal syndrome which may be accompanied by hiccoughs.—*M. L. Sussman.*

DELHERM, L., DEVOIS, A., and RULLIERE (Mme.). Etude des gros vaisseaux de la base du coeur par les méthodes radiologiques d'examen "en coupe." (A study of the great vessels at the base of the heart by sectional roentgenography.) *J. de radiol. et d'électrol.*, April, 1939, *23*, 145–156.

A horizontal planigraphic method is described with a tube being displaced through an arc of a circle whose diameter equals 15 to 20 cm. The kilovoltage equals 85 to 100, distance 1 meter, 50 to 70 ma., time 2 to 3 seconds in the left lateral position and 0.8 to 1 second in the anteroposterior position. Exposures are made centimeter by centimeter going from the left hilum to the right hilum. A comparison of the ordinary views with the planigrams of the same cases is given accompanied by sketches. These show the appearance of normals, of calcareous plaques in the aorta, small localized dilatations of the aorta, and the possibility of similar investigation of pulmonary artery disease is suggested.—*M. L. Sussman.*

DELHERM, L., DEVOIS, A., and RULLIERE (Mme.). Etude des gros vaisseaux de la base du coeur par les méthodes radiologiques d'examen "en coupe." (Study of the great vessels at the base of the heart by sectional roentgenography.) *J. de radiol. et d'électrol.*, Aug., 1939, *23*, 337–347.

In a previous article the authors described the various findings in disease of the aorta. Here they show the value of this method in determining the condition of the pulmonary artery. The sections were made successively 1 cm. apart from one hilum to the other with the patient in the lateral position. Three examples are presented, illustrating dilatations of the pulmonary artery. The information obtained in the sectional study appears distinctly more diagnostic than by the ordinary roentgenograms. A case of mediastinitis is also described in which the sections permitted an estimate of the heart size. Mediastinal tumors apparently also would lend themselves to this type of examination.—*M. L. Sussman.*

ABDOMEN

SINGLETON, ARTHUR C. Chronic gastric volvulus. *Radiology*, Jan., 1940, *34*, 53–61.

Volvulus of the stomach may be upward around the long axis of the stomach or from right to left or left to right around the long axis of the gastrohepatic omentum. The former type is the more frequent.

The clinical picture of acute total volvulus of the stomach is that of early vomiting followed by violent retching and inability to vomit; the stomach tube cannot be passed and meteorism of the epigastrium develops rapidly. This indi-

cates obstruction at the pylorus and then at the cardia, followed by distention of the stomach.

Three cases are described and illustrated with roentgenograms. In 2 there was persistent volvulus with interposition of the colon between the liver and diaphragm and in the third intermittent volvulus alternating with anterior interposition of the colon between liver and diaphragm. The roentgen picture of chronic gastric volvulus is so characteristic that it is not apt to be confused with that of any other condition. The colon should be examined in all suspected cases to exclude simple displacement of the stomach by a distended colon. All of the 3 cases described here had abnormally high colons, but they were not distended. Apparently, in the first 2 cases at least, the colon was dragged up by the rotated stomach, instead of having caused the rotation.

The chief factor in total volvulus is an abnormally long gastrohepatic or gastrocolic omentum, probably congenital in origin. A rotated stomach may return to its normal position spontaneously, as shown in Case III.—*Audrey G. Morgan.*

MacCarty, Wm. C. Cancer of the stomach. *Radiology*, Jan., 1940, *34*, 1–7.

The author, in giving the Carman Lecture, paid tribute to his friend Dr. Carman and reviewed the progress in the treatment of stomach cancer since the introduction of roentgenology and fresh tissue cytology. Before the beginning of this century the pathological work on cancer was done on postmortem material and the conclusions were largely guess-work.

In 1908 the author, in collaboration with Dr. L. B. Wilson, studied 153 cases of carcinoma of the stomach and found sufficient evidence to justify their saying that 71 per cent of them had developed in ulcers. This tells nothing about the number of ulcers that undergo cancerous degeneration and that may never be known. But in 1914 MacCarty published a detailed description of cell changes in the borders of ulcers which he calls "secondary cytoplasia." This picture is quite different from that of ordinary cellular reparative regeneration. A diagram is given showing the difference. The cells in secondary cytoplasia have all the morphological characteristics of cancer cells but they are still in the tubules. They do not necessarily invade the surrounding tissues, but it is impossible to tell in advance whether such tissue invasion will take place. He thinks it safe to say that all chronic gastric ulcers are potentially cancerous and that at least 90 per cent of them over the size of a quarter (2.5 cm. in diameter) are definitely cancers.

He has found cancers as small as 1 cm. in diameter and has recently reported 121 cases less than 2.5 cm. in diameter. The average size of operable cancers diagnosed is 6.1 cm. and 75 per cent of gastric cancers are inoperable when first seen, which suggests that much more thorough work must be done in the early diagnosis of cancer of the stomach. A careful roentgenoscopic examination should be made of any patient with upper abdominal symptoms. If ulcer is found operation should not be delayed too long if it does not disappear. Even if it does the patient should be kept under roentgenoscopic observation for some time for even in the hands of the best experts ulcers that have been diagnosed as benign have proved on resection and examination to be malignant.—*Audrey G. Morgan.*

Hochmann, A. Sarcoma of the stomach. *Lancet*, Feb. 24, 1940, *1*, 362–363.

Two cases of sarcoma of the stomach are reported. One was treated with roentgen therapy and improved, the patient being able to return to work as a painter and being in excellent health some three years and still living. The other patient was treated surgically and died. In both cases, the diagnosis was established by histological study of tissue removed by operation. In the first case, the tumor was so widely infiltrated that it was considered inoperable. Therefore, the surgical treatment was limited to biopsy and thereafter a total of 3,000 r was administered through three fields (150–200 r per treatment—other factors not given). Subsequent roentgenography visualized involution of the lesion. In the second case, the lesion was smaller and partial gastrectomy, including removal of glands in the lesser omentum, was performed, the patient dying several days later.

In discussion, the author cites the rarity of sarcoma of the stomach—approximately 1 per cent of all gastric tumors. Its incidence begins at twenty to thirty, rises steeply, with an average age about forty-six, and falls rapidly in the seventh decade. The lesion may grow exogastrically or endogastrically. Usually, sarcomatous lesions, when studied, are larger than carcinomatous lesions. There may be no symptoms or pain, vomiting and gastric hemorrhage may occur. Roentgenologic evidence is not specific;

therefore, laparotomy and biopsy should be accomplished whenever a non-epithelial tumor is suspected.—*A. A. de Lorimier.*

CORREIA NETO, A. Achalasie du pylore chez l'adulte. (Pyloric achalasia in the adult.) *Presse méd.*, Feb. 6, 1940, *48*, 148–153.

Achalasia of the pylorus in the adult is defined as that pathological condition characterized by chronic gastric stasis with muscular hypertrophy of the gastric wall, hyperperistalsis and delay in gastric emptying. It is not necessary to find evidence of organic stenosis of the pylorus, intrinsic or extrinsic, either roentgenologically, operatively or by postmortem. The disease is considered to be the same as the pyloric stenosis of the newborn, but the clinical symptoms of the latter condition are lacking. The condition is relatively common; it is considered rare only by those who insist on a pyloric tumor as a feature of the disease. Megaesophagus and megacolon are often found in association with this condition and are probably of the same etiology. Pathogenesis is discussed in detail. The conclusion of the author is that an achalasia and not a spasm of the pylorus exists and may be attributable to a lesion of Auerbach-Meissner plexus following on a chronic lack of vitamin B_1. An important pathological consideration is the fact that the pylorus itself is not hypertrophied. This change is limited to the prepyloric segment.

The diagnosis is based upon the clinical picture of chronic gastric stasis. There is no stenosis of the pylorus. Other causes of gastric stasis must be excluded such as cicatrizing duodenal ulcer, gastric carcinoma, stenosis due to extrinsic or congenital causes, chronic duodenal stasis, etc. It is important to make the surgeon aware of the syndrome else he miss a localized hypertrophy of the muscle wall in the absence of pyloric stenosis. Treatment is surgical, preferably by pyloroplasty.

The author gives the clinical history and operative findings completely in 5 cases.—*M. L. Sussman.*

BOON, THOMAS H. Intubation of the small intestine; demonstration and localisation of partially obstructive lesions. *Lancet*, Jan. 6, 1940, *1*, 7–10.

The Miller-Abbott tube has provided for decompression of a distended bowel, the restoration of body fluids and electrolytes (orally), the establishment of drainage proximal to the site of obstruction, the use of barium for detailed study of the tract and finally, it has provided for leisurely handling of the case while developing a decision as to the proper definitive measures.

Nine cases are presented to emphasize the application of the tube not only in frank cases of obstruction but also for cases of partial obstruction due to narrowing, angulation, persistent spasm and the like.

Movement of the tube was checked roentgenoscopically. When the balloon became arrested for as long as two hours, barium was injected. The mixture was 2 parts water to 1 part barium. Normally, when the balloon is inflated with 30 cc., its movement along the tract is slowly progressive without interruption until reaching the ileocecal valve. Very little regurgitation of injected barium occurs except right at the site of obstruction or at the ileocecal valve. Evidence to the contrary or the direct visualization of a persistent narrowing of the lumen, distal to the shadow of the balloon, served to establish diagnosis of obstruction. Distinction between organic vs. functional obstructions remains difficult. Permanent arrest of the bowel contents usually indicates some localized pathological process. The evidence of disturbance of function (regurgitations) is considered to be of value equal in importance to anatomical abnormalities—hence the importance of noting the behavior of the barium injected with the balloon deflated.—*A. A. de Lorimier.*

GERSHON-COHEN, J., and SHAY, HARRY. Ileocaecal tuberculosis. *Am. Rev. Tuberc.*, Nov., 1939, *40*, 595–598.

The authors describe a procedure for directly studying the small intestine without the usual delay incurred with the barium meal or the barium enema. They pass a duodenal tube and after the tip of it has progressed beyond the second portion of the duodenum, a barium suspension is injected by gravity or by means of a syringe until the desired portion of the intestine is filled. Air may be added at any time and thus a double contrast obtained. Ordinarily 400 to 800 cc. is required to visualize the small intestines. Filling may be continued at least to the splenic flexure. This method of study has been particularly valuable for demonstrating lesions of ileocecal tuberculosis. Four reproductions are included.—*A. A. de Lorimier.*

Rachet, J., and Arnous, J. Une méthode nouvelle d'étude radiologique du côlon, les radiographies en série. (A new roentgen method for the study of the colon: serial roentgenography.) *Presse méd.*, July 8, 1939, *47*, 1093–1096.

The patient is prepared by a saline irrigation in the evening before the examination and a second and even a third irrigation the following morning. The barium mixture must be homogeneous and run in slowly at a temperature of 37° C. Peristalsis of the colon is activated by a subcutaneous injection of prostigmine. The substance is injected after partial evacuation sometimes followed by the injection of a small amount of air. The patient is placed into the position fluoroscopically which best shows the area to be studied. Five to eight roentgenograms are made at regular intervals, ordinarily every ten minutes. The method is based upon the assumption that an organic lesion will remain constant in position and outline while peristalsis elsewhere will change the configuration. It is believed that the method offers an appreciation of the extent of the lesion, of its operability and some information on its nature. —*M. L. Sussman.*

Oury, P., and Peraly, E. Les troubles gastriques au cours du dolichocolon. (Gastric disorders associated with dolichocolon.) *Presse méd.*, June 17, 1939, *47*, 964–966.

The authors describe three forms: the dyspeptic, pseudo-ulcerous and stenosing. In the dyspeptic form the patients complain of such symptoms as post-prandial heaviness, nausea, vomiting and odorous breath. Symptoms such as these, associated with a long standing constipation or episodes of abdominal pain, are indications for a barium enema to determine the presence of an elongated colon. In the second group are patients whose symptoms are those of ulcer but roentgen examination of the stomach fails to confirm this diagnosis. However, the pain described is more irregular, less violent and without the periods of freedom characteristic of the ulcer. Vomiting is not as frequent; hematemesis, however, is not uncommon. In the third form distention of the elongated colon by gas sometimes provokes symptoms of gastric compression or stenosis. There may be stasis up to six hours. Finally marked gastric deformities are found, sometimes rotated or inverted with pylorus and antrum behind the stomach.—*M. L. Sussman.*

Kleeberg, J. Radiological diagnosis of tumors of the pancreas. *Lancet*, March 9, 1940, *1*, 453–454.

Engel and Lysholm described visualization of a tumor of the pancreas after administering an effervescent powder to the patient thereby filling the stomach with gas.

The authors have modified this technique to the extent of using a stomach tube (Ryle or Einhorn) with a soft rubber balloon tied to the tip of it. This balloon is inflated through perforations in the tubing, after positioning it to the pyloric extremity of the stomach; 400–600 cc. or even as much as 800 cc. of air may be pumped into the tubing by means of a 50 cc. syringe. After roentgenography, the air is simply released and the tubing and balloon easily removed. More than thirty such examinations have been conducted without a mishap.

Normally with this technique the pancreas and large vessels are visualized, particularly in the lateral position, as a small, straight and slightly dense shadow between the vertebral column and the air-filled stomach. A tumor appears as a large dense round shadow, in the anteroposterior position, or as a very prominent density between the vertebral column and the gas filled stomach in the lateral projection. In case the tumor were an aneurysm its pulsations would be evident.

During the inflation of the balloon, pain was complained of by only 2 patients. Both were later found to have carcinoma of the stomach. The author suggests that stretching pains may constitute a very early sign of cancer of the stomach.—*A. A. de Lorimier.*

Cashion, William R. Pericolic membranes. *Radiology*, Jan., 1940, *34*, 66–68.

The author presents this paper to show that pericolic membranes have a definite roentgen picture. According to Duffield they "are undoubtedly congenital and consist of a reduplication of the parietal peritoneum extending up the side of the cecum and frequently around the lower end of the cecum and here having a tendency to shorten the meso-appendix and produce strangulation." In 1932 he published a survey of 200 cases in 10 per cent of which appendectomy had been performed. These cases were sent for roentgen examination and showed moderate to marked pyloroduodenal spasm with no filling defect; moderate six hour stomach residue in most cases; ileocecal delay due to the acute angle at which the ileum entered the

cecum; smooth deformity of the cecum and spasm of the transverse and descending colon. Haustral markings absent or shallow. In some cases the membranes extended up to the hepatic flexure and caused a sharp angulation and reduplication in that region.

Secondary operation was performed in these cases and the patients were completely cured. In a few months they had gained enough weight to take care of the enteroptosis which often exists in such cases; in a few cases, however, there was such marked ptosis that it had to be given special treatment.—*Audrey G. Morgan.*

SARALEGUI, J. A. Découvertes radiologiques dans l'exploration des voies biliaires. (Roentgenologic findings in the exploration of the biliary tract.) *J. de radiol. et d'électrol.*, Jan., 1939, *23*, 1–14.

The author is convinced of the clinical and functional value obtained from contrast visualization of the biliary tract. Although the study can be made immediately at the operating table he prefers the postoperative method in which several days elapse after the operative fistula has been created through the gallbladder or common duct.

A thorium solution is employed because of its excellent miscibility with the biliary fluid. Under roentgenoscopic observation it is allowed to flow through the fistula without force if possible. The aim of the procedure is to study the morphology and function of the biliary ducts. It is felt that thereby the number of duodenostomies will be considerably reduced.

The normal gallbladder fills easily and shows a slight delay to passage at what is interpreted as a cholecystic sphincter. Contractions ensue and emptying occurs gradually until the sphincter relaxes completely. At this time the cystic and common ducts begin to be visualized. A second, longer delay occurs at the sphincter of Oddi. This is accompanied by regular, slow contractions. The hepatic ducts may be filled by exerting pressure on the injecting syringe. In the author's experience visualization of the ampulla of Vater is usually of pathological significance.

In biliary lithiasis residual stones may be brought into relief. A warning is made against the inclusion of air bubbles. In cases of obstruction the miscible solution outlines the stone by virtue of its ability to penetrate on all sides. In obstruction in the common duct tremendous dilatations of the duct may occur. Calculi lodged at the level of the sphincter ordinarily allow a small amount to pass. If located in the ampulla the stone may be hidden by overlying opacity filling the duodenum. Once the calculi have been removed, repeated examinations show a diminution in extent of the dilatation.

The findings in hepatobiliary dyskinesis were obtained by a study of 68 cases of non-calculous chronic cholecystitis and are as follows: (1) small gallbladder; (2) hyper-peristalsis; (3) active cholecystic sphincter; (4) active contractions of cystic and common ducts; (5) sphincter of Oddi in state of contraction with slight dilatation of the ducts indicating stasis; (6) conical sphincteric canal with variably irregular contour. When this latter finding is persistent, especially if accompanied by hyperperistalsis, it is suggestive of an organic lesion such as chronic stenosing pancreatitis. Antispasmodics act on the functional type, and increasing of the pressure of the flow causes pain.

Non-calculous, organic obstructions, such as retractile and stenosing Odditis, show only slight dilatation of the common duct. The intrapancreatic canal is short and conical with smooth walls. The flow is slow in the terminal segment and occasionally a clear space is noted between the sphincter and the duodenum. In carcinoma of the head of the pancreas obstruction of the common duct appears early and causes moderate dilatation. The distal segment is conical, ends abruptly and shows a smooth, convex margin. If the duodenum is filled a hiatus is observed. The duct of Wirsung is not visualized. Carcinoma of the papilla produces a similar appearance except for an irregularity of the terminal segments.—*M. L. Sussman.*

GENITOURINARY SYSTEM

MACQUET, P., and LECOQ, P. Les rétrécissements congénitaux de l'uretère. (Congenital stenosis of the ureter.) *Presse méd.*, March 22, 1939, *47*, 439–442.

Congenital ureteral stenosis is a rare disease although probably more common than is generally suspected because it is not discovered until pyonephrosis occurs with a masking uremia. There are three physiological narrowings of the ureter: at the ureteropelvic junction due to embryological rotation of the kidney; at the superior inlet of the pelvis, and in the intramural portion of the ureter. In addition to a pathological accentuation of the physiological

narrowing, valves occur in ureters which otherwise appear normal. The sites of predilection are at these same physiological levels. They are explained as originating in fetal folds. In most cases the site of narrowing is fairly permeable until there is a superimposed inflammation. There is considerable debate as to whether most cases show one or more stenoses. Above, the ureter is dilated, there is dilatation of the pelvis and calyces and ultimately atrophy of the kidney. Below, the ureter is normal or perhaps contracted. In the presence of infection pyoureteral nephrosis occurs which progresses rapidly and leads to renal death.

There are no symptoms referable directly to the stenosis. The symptomatology is dependent upon retention, mild or considerable, and superimposed infection. Ureteral catheterization is of value in diagnosis. Descending pyelography does not give definite evidence of the caliber or extent of the stenosis. Ascending pyelography is the most useful procedure in the diagnosis. None of these procedures determine the cause of the lesion. Extrinsic pressure, tumor, secondary cicatrization due to abdominal inflammation, renal neoplasm, roentgen or radium therapy, fracture of the pelvis or spine must be excluded by any available means. Spasm must be differentiated from peristaltic waves by repeated examination.—*M. L. Sussman.*

SKELETAL SYSTEM

Jaubert de Beaujeu, A., and Benmussa. Synostose astragalo-scaphoïdienne congénitale, bilatérale et isolée. (Congenital astragaloscaphoid synostosis, bilateral and isolated.) *J. de radiol. et d'électrol.*, Aug., 1939, *23*, 348–352.

Only 7 cases of this condition have been reported in the literature. Of these, 6 were unilateral and one bilateral, and all except one were accompanied by other abnormalities of the bones of the feet. The French textbooks of anatomy by Testret and Poirier do not mention this anomaly. The authors' case was that of a man, aged twenty-three, with bilateral narrowing of the astragaloscaphoid joints. Only a faint line of demarcation remained between the two bones. There was no evidence of recent or old disease.—*M. L. Sussman.*

Passebois, P., and Betoulieres, P. Ostéochondrite vertébrale infantile ("vertebra plata" de Calvé). (Infantile vertebral osteochondritis ("vertebra plana" of Calvé).) *J. de radiol. et d'électrol.*, Sept., 1939, *23*, 397–400.

A detailed history and follow-up of a case of vertebra plana, originally described by Calvé, is presented. Repeated roentgen examinations during the three years of observation demonstrate the evolution of the process and its response to therapy. The involved vertebral body showed considerable flattening. Healing occurred by ossification above and below the compressed body. Several elements in this case which have not been reported previously are worthy of mention: (1) The presence of a fusiform soft tissue mass about the diseased body, simulating a cold abscess. This disappeared later. (2) A pinching of the adjacent vertebral discs.—*M. L. Sussman.*

Passebois, P., and Betoulieres, P. L'aspect radiologique des encoches du corps vertébral de l'enfant. (The roentgen picture of the notch in the vertebral body of the infant.) *Presse méd.*, Feb. 18, 1939, *47*, 280.

This article concerns the anatomical basis for the notch seen on the anterior border of the vertebra in the lateral view which gives it the appearance of the head of a tortoise. The notch appears at the age of four to five months, becoming progressively more prominent up to the age of fifteen to twenty months. They are seen only in the dorsal vertebrae and disappear progressively in size and number. They disappear in order from the ends of the dorsal spine toward the center. The fifth, sixth and eighth dorsal vertebrae are the last to lose this appearance usually at the age of sixteen or seventeen years.

It is usual to interpret the appearance as due to a vascular pedicle, but it is difficult to understand why they are not seen in the lumbar vertebrae where anatomically the appearance should not be different. The authors point out that there is a disproportion between the small vessels entering the anterior surface of the vertebral bodies and the notch. Their studies suggest that the notch is due to the existence in the vertebral bodies of two cells appearing as flattened spheres faced one against the other at the median line and containing a dense medullary tissue. The nature of this tissue is undetermined although it is suggested that it is related in some way to blood formation.—*M. L. Sussman.*

POTOZKY, HENRY, and FREID, JACOB R. Ewing's tumor simulating sarcoma of soft-tissue origin. *Am. J. Cancer*, May, 1939, *36*, 1–11.

Ewing's sarcoma (endothelial myeloma) is generally considered to arise from endothelial cells. Recently, there has been evidence which suggests that instead of this origin, it might arise from undifferentiated mesenchyme. Particularly when involving very young individuals it becomes manifest as an osteomyelitic process. Soft tissue lesions are usually secondary. The author is presenting 4 cases in which a soft tissue mass was the conspicuous evidence.

The first case was that of a female, aged twenty-four, who had had a soft tissue tumor (about 6 cm. in diameter) removed from the left upper scapular region in 1930. A local recurrence was noted in 1933 and in 1934 she developed a left-sided pleurisy with effusion. This was treated in a tuberculosis sanatorium (sputum was persistently negative). In 1935 a large mass presented in the left supraspinous fossa. This was treated with extensive roentgen irradiation and it receded completely. Small nodular regrowths appeared in about seven months. These progressed rapidly in size, regardless of irradiation and the patient died six and one-half years after the first evidence of the tumor. Autopsy revealed a tumor of a pattern which was similar to Ewing's sarcoma.

The second case was that of a female, aged forty, having sciatic symptoms. A mass was palpated in the left sacroiliac region, though roentgen studies of the pelvis were negative. Roentgen therapy relieved the symptoms and the tumor receded, but after six months the sciatic symptoms returned. A biopsy was attempted by punch approach through the perineum and the patient died shortly thereafter. Autopsy revealed a retroperitoneal tumor in the left sacroiliac region with superficial involvement of the adjacent bones and with metastases throughout the lungs. Microscopically, the tumor presented the appearance of Ewing's sarcoma.

The third case was that of a male, aged fifty-two, admitted because of a mass in the right sternoclavicular region, which he claimed to have had for some ten years—but which had grown rapidly during the past year. This mass measured approximately 5×5 cm.; it was firm and appeared to be attached to the clavicle. Roentgen studies did not indicate any involvement of the clavicle. The biopsy report was "hemangio-endothelioma"—later considered to be endothelial myeloma. A radium pack was applied (35,000 mg-hr. administered fractionally over a period of six days). The mass completely disappeared and there was no evidence of recurrence until three years later when some destruction of the clavicle was noted. After one additional year, it was found that the clavicle was markedly destroyed, and nodular lesions were visualized in the lungs. Roentgen therapy was administered to all lesions and regression resulted. The patient is still living, five and one-half years after the initial treatment.

The fourth case was of a male, aged thirty-four, who died one week following admission to the hospital. He had had a "ganglion" removed from his left ankle eight years previously (no histological studies). Six months later, a firm movable tumor appeared at the operative site. A biopsy was performed two years thereafter; this revealed a "round cell sarcoma." Some deossification was noted in the fibula and lesions were found in the lungs. Roentgen therapy given at that time accomplished involution of all known lesions but three years later a recurrence was noted in the ankle. An amputation was performed below the knee. A year later, a mass developed just above the knee. Biopsy was performed and the report was "Ewing's sarcoma." Roentgen therapy was given, but within a few months a transverse myelitis developed and the patient died after incurring a decubitus ulcer and sepsis—eight years following the first notice of his tumor. Autopsy revealed metastases in ribs, vertebrae, right femur, lungs, liver, pancreas, suprarenal and numerous lymph nodes. In the bones, the neoplasm was mainly associated with the haversian canals and extended subperiosteally. The structure was typical of Ewing's sarcoma.—*A. A. de Lorimier.*

WEIL, P. E., and PERLES, S. L'examen clinique des maladies des os; les radiographies d'ensemble du squelette et les ponctions osseuses répétées. (Clinical examination of bone lesions; roentgenograms of the entire skeleton and repeated bone punctures.) *Presse méd.*, July 12, 1939, *47*, 1102–1104.

The authors review the application of sternal puncture and skeletal roentgenography in the diagnosis and understanding of Gaucher's disease, myeloma and secondary carcinoma. The

bone punctures are made either at the site of the localized tumor, in the sternum or spine. These procedures contribute considerably to the early diagnosis.—*M. L. Sussman.*

Forestier, J., and Metzger, J. La clef du diagnostic précoce de la spondylarthrite est dans la radiographie des articulations sacro-iliaques. (The key to early diagnosis of spondylarthritis is in roentgenography of the sacroiliac articulations.) *Presse méd.*, Aug. 16, 1939, *47*, 1247–1249.

The authors have been interested in demonstrating the basic clinical diagnosis of ankylosing spondylarthritis of Pierre Marie in the preankylosing stage. They believe that the early signs may be found in the sacroiliac joints. Reviewing 159 cases of this condition examined during the evolution of the disease only 2 cases were shown in which the sacroiliac joints were roentgenologically normal. Changes in the sacroiliac joints were found to precede those in the spine. For the examination an anteroposterior view was made. Changes are found early, not in the joint outlines themselves but in the subchondral portions of the adjacent bones. First there is a pseudo-enlargement of the articular space with marginal decalcifications. The zone of the calcification is then replaced by a mottling which gives the trabecular structure a spotted appearance. Finally the joint space disappears and there is synostosis.—*M. L. Sussman.*

Weissenbach, R. J., and Lievre, J. A. Les ostéites fibreuses sans adénome parathyroïdien. (Osteitis fibrosa without parathyroid adenoma.) *Presse méd.*, Feb. 18, 1939, *47*, 260–262.

These conditions may be grouped as follows:

1. Paget's disease.
2. Juvenile, localized fibrocystic osteitis, otherwise known as single or multiple bone cysts. The multiple lesions are apt to occur in the proximal ends of the femur and humerus.
3. Bone lesions in neurofibromatosis.
4. Disseminated fibrous osteitis with pigmentation and endocrine disorder of the type described by Albright.

There are other cases of extensive osteitis fibrosa which are slowly progressive and which have no distinctive characteristics other than absence of all signs of parathyroid hyperfunction.—*M. L. Sussman.*

BLOOD AND LYMPH SYSTEM

Baker, Charles, and Mann, W. N. Hodgkin's disease. *Lancet*, Jan. 6, 1940, *1*, 23–25.

During the past few years much trust has been given the Gordon test for establishing the diagnosis of Hodgkin's disease but it now appears that positive reactions by this test are dependent upon eosinophilic content of the tissue.

The author is summing up his convictions about this disease on the basis of observations of 65 cases seen at Guy's Hospital between 1926 and 1937. These 65 cases are selected because in them the diagnosis was established either by biopsy or autopsy studies; many other cases had been diagnosed "Hodgkin's disease" but they were not included in the analysis because they lacked histological studies and the author has too often seen contradiction to mere clinical diagnoses.

Of this accepted series, 47 were males; 18, females. In half of the cases, the age of onset was during the second and third decades; only 4 cases occurred after the age of sixty. In only 7 cases was there any history of chronic enlargement of the lymph nodes and in only one case was pulmonary tuberculosis actually noted. Apparently the relationship between tuberculosis and Hodgkin's disease has been overemphasized. The cervical glands are usually the first to actually show involvement; involvement of deeper glands appeared to be a sequel. Splenic enlargement was noted in 35 out of the 65, while enlargement of the liver was noted in 30. Jaundice occurred in only 2 cases. Pruritus was a symptom in 13 cases, but skin deposits of Hodgkin's tissue were found in only one. Eight cases showed symptoms of nervous tissue involvement but lesions were found only in and about the spinal cord and peripheral nerves. There were no gross lesions of the brain. There appeared to be no typical blood picture; 16 cases showed a leukocytosis of over 8,400 while a leukopenia was found in only 4 cases. An eosinophilia of 5 per cent or more was seen in 11 cases. Anemia was invariably present in those with general symptoms, such as fever. Fever was notable in 35 cases but of these only 3 had cervical node involvement. The others had disease of the mediastinum, lung or abdominal lesions. In 21 cases, the fever course was the characteristic Pel-Epstein type. If given roentgen therapy the average duration of life was three years, otherwise eighteen months.

Apparent cure was effected in 2 cases after surgical excision of cervical glands combined with deep roentgen therapy.—*A. A. de Lorimier.*

GENERAL

JONSCHER, K. L'étiologie et la pathogénie des toxicoses des nourissons. (The etiology and pathogenesis of the toxicoses in infants.) *Presse méd.*, April 15, 1939, *47*, 583–586.

Two principal theories are suggested in the literature. In one a defective alimentation is assumed to be present interfering with digestion and assimilation and permitting intoxication. It is pointed out that the disease occurs irregularly and always in artificially fat infants. A proper regimen cures the patient even in severe cases. Pathologic examination reveals no localizing lesion. The second theory assumes infection as the cause which may be evident or hidden. Colitis and otitis are claimed to be definite causes of toxicosis. No single organ has been isolated. Furthermore, the intestinal mucosa fails to show any definite lesion. Otitis, on the other hand, is recognized as a definite factor in the etiology. Clinical evidence abounds in proof of this statement. It is probable that a compromise of both theories explains the observed facts and that cases can be divided into three groups, those purely alimentary, those with a predominance of infection but with an existing disturbance in metabolism in addition, and in mixed forms.

There is a circulatory disturbance which consists of both an actual and relative distribution in the quantity of circulating blood. As a result there is noted roentgenographically, the author states, a lowering of the diaphragm and a small sized heart. Gross measurements of the volume of the heart made and compared with the volume of the lungs confirms this finding. The changes are partly due to dehydration and partly to stasis of blood in the abdominal organs.—*M. L. Sussman.*

TROSTLER, I. S. Contributory negligence as it applies to medical malpractice. *Radiology*, Jan., 1940, *34*, 76–81.

The author thinks that in defense against malpractice suits physicians and their lawyers could make much more use than they do of evidence of contributory negligence on the part of the patient. Of course the patient cannot be expected to know the meaning and value of some of the things that he is instructed by the physician to do. But if directions are given definitely and in detail and the patient fails to obey them and harm results, he is responsible on the ground of contributory negligence even if there has been a certain degree of negligence on the part of the physician also. The author has always emphasized the importance of physicians keeping careful records of cases and giving concise and adequate instructions to the patients, or their guardians if they are minors. Cases are cited in which proof of contributory negligence on the part of the patient won a decision for the physician, as, for instance, refusal of a patient to have an x-ray taken.—*Audrey G. Morgan.*

ROENTGEN AND RADIUM THERAPY

DEUCHER, W. G. Die Wiederherstellung der normalen Aktionsfähigkeit des Patienten als Ziel der Strahlenbehandlung bei Fernmetastasen. (The restoration of the normal activity of the patient as the object of irradiation in distant metastases.) *Strahlentherapie*, 1940, *68*, 537–586.

In judging the effect of radiotherapy in the treatment of distant hematogenous metastases there are three things to consider: (1) the palliative local improvement; (2) the lengthening of life, and (3) the lengthening of the patient's capacity for activity and his feeling of well being. The author uses the word eupathia to express this.

From this point of view he reports the results of treatment at the Therapeutic Roentgen Institute of the University of Zurich from January 1, 1930, to January 1, 1940. The total number of cases was 432, 201 in men and 231 in women. The average age was 55.3 years; the youngest patient was one year old, the oldest seventy-nine when the metastases were diagnosed. Tables and graphs are given showing the details of the results.

Among 181 cases of lung metastases 28 per cent were irradiated and good local results attained in 61 per cent. The length of life of the irradiated patients was on an average seven months longer than that of the non-irradiated ones. The effect on the duration of the eupathic period was still better, for the average eupathic period of the irradiated patients was 6.4 months while the non-irradiated ones remained well for only 1.2 months. The percentage of patients who became eupathic was considerably in-

creased by irradiation. Among the patients who became eupathic after irradiation the length of the eupathic period in proportion to the duration of life was greater than among the non-irradiated ones.

Among 385 bone metastases in 208 patients 72 per cent were irradiated and good local effects were obtained in 78 per cent of these. The life of the irradiated patients was on an average six months longer than that of the non-irradiated patients. The length of the eupathic period of the irradiated patients was on an average 5.9 months while that of the non-irradiated patients was only 0.75 month. The percentage of eupathic patients among the irradiated ones who lived for six months was 36 per cent while among the non-irradiated it was only 13 per cent; among those living after twelve months 33 per cent of the irradiated patients were eupathic and none of the non-irradiated ones. Among patients with bone metastases from tumors of the testicle, breast and prostate particularly, the length of eupathia was almost coincident with that of life.

Among 80 cases of skin metastases 68 per cent were irradiated and in 76 per cent of these the local results were good. The average life of the irradiated patients was three times as long (15.8 months) as that of the non-irradiated ones (4.6 months). The average duration of eupathia among the irradiated was 4.5 months and among the non-irradiated only 0.4 month. After six months 36 per cent of the irradiated patients were still eupathic and only 13 per cent of the non-irradiated ones.

Among 81 patients with metastases in the liver, brain, soft parts and eyes, 28 per cent were irradiated and good local results attained in only 14 per cent of these. The average life of the irradiated patients exceeded that of the non-irradiated by only 1.1 months. The duration of the eupathia in both irradiated and non-irradiated was less than one month. Among the irradiated patients living after six months none were eupathic, while among the non-irradiated ones 12 per cent were still active.

It is evident from the figures that eupathia can be increased by irradiation given on proper indications. This point should be considered in future statistical material.

Irradiation is absolutely indicated in lung metastases from seminoma of the testicle and Langhans malignant goiter, hilum metastases and painful carcinomatous pleurisy from all primary tumors except tumors of the mouth, pharynx and esophagus; in bone metastases from primary tumors in the thyroid, breast and testicles and female genitalia; in skin metastases from all primary tumors when no other metastases are demonstrable.

Irradiation may be tried in solitary lung metastases from tumors of the skin, the thyroid, breast and prostate; in multiple lung metastases from tumors of the testicle, the thyroid and of the breast in some cases; in painful bone metastases from all primary tumors; in skin metastases from tumors of the breast and in other metastases if they cause intense pain.

Irradiation seems to be contraindicated in multiple lung metastases except those mentioned above; all lung metastases from tumors of the mouth, pharynx and esophagus; bone metastases from tumors of the lungs, the mouth, the pharynx and of melanomas if they do not cause intense pain; all other metastases except those mentioned above under indications.—*Audrey G. Morgan.*

Levin, Isaac. Pathogenesis and radium therapy of mixed tumors of the salivary glands. *Radiology*, Jan., 1940, *34*, 69–75.

The author has studied 26 cases of mixed tumors of the salivary glands, clinically and microscopically before and after treatment. Five cases are described and illustrated with photomicrographs. These tumors develop from the undifferentiated cells of germinal rests which are capable of producing cells of any germinal layer. For that reason they are necessarily radiosensitive.

Unlike mixed tumors of the ovaries and testicles they grow slowly and are often benign, but as they frequently recur after either surgery or radiotherapy and may suddenly take on rapid malignant growth, every one must be considered potentially malignant and treated accordingly.

As they grow slowly, intensive treatment is not necessary. The author excised the tumor and immediately inserted radon capillaries into the field of operation (from 4 to 8 capillaries each containing 1 mc.). The wound was then closed and small blocks of radium, about 100 mc-hr. at each treatment, applied to the surface. The surrounding tissue must be protected so that another treatment can be given if the tumor recurs.

The material is not large enough to serve as the basis for a statistical report of results. In one case recurrence took place eleven years after the

beginning of treatment. In one case autopsy eleven months after the beginning of treatment —death from cerebral hemorrhage—showed no tumor tissue. In one case ulcers of the skin caused by the tumor healed. In almost all of the cases the tumor decreased in size promptly after treatment.—*Audrey G. Morgan.*

PATERSON, RALSTON, and NUTTALL, JOHN R. An evaluation of the risk of biopsy in squamous carcinoma. *Am. J. Cancer*, Sept., 1939, *37*, 64–68.

Comment is made as to the conflicting reports descriptive of clinical and experimental studies which pertain to dissemination of neoplastic cells because of biopsies.

The authors have analyzed their results in 166 cases of which 99 were subjected to biopsy. All their cases were squamous cell carcinoma, superficially located—either in the skin, or on the mucous membranes of the mouth. This type of case was selected because of the following requirements: (1) that there be no trauma associated with the treatment; (2) that there be no known metastases at the time of biopsy or treatment; (3) that the characteristic path of metastasis be discernible; (4) that the tumor be of a type likely to respond to roentgen therapy; (5) that reasonable diagnosis be available for the control cases (utilizing surface ulcerations); (6) that final judgment be delayed until ample time allowance for metastases to take place.

Of the cases selected on this basis, 19 per cent of those which were biopsied developed metastases, while 20.5 of those which were not biopsied did likewise. The authors emphasize their opinion that biopsies do not increase the likelihood of metastases; moreover, that they provide for adequacy of treatment of the patient and the gaining of information for improving methods of treatment in the future.—*A. A. de Lorimier.*

BINKLEY, J. SAMUEL. Aspiration biopsy of tumors of the liver. *Am. J. Cancer*, June, 1939, *36*, 193–200.

Shortcomings are cited as to various methods of studying the liver: function tests; pneumoperitoneoscopy; the use of thorotrast, etc. Mention is made as to the experiences of others in performing liver punctures. The author has performed these on 19 cases. In 73.6 per cent the procedure served to establish the diagnosis. It is recommended for studying selected tumors of the liver, such as where malignancy is suspected in a superficial mass, though no neoplasm can be found elsewhere; where the primary lesion has been eradicated.

As far as the technical procedure is concerned, the author stresses several considerations: (1) preliminary decompression of the bowel (by catharsis enemata); (2) preliminary abdominal paracentesis, in cases of ascites (and study of the fluid for malignant cells); (3) the use of the abdominal rather than the intercostal approach. The patient is placed in the semirecumbent position. The skin is antiseptically prepared and a No. 17 gauge aspirating needle is inserted with negative pressure. Several cubic centimeters of blood can be expected. It should be coagulated and studied for neoplastic cells. If a sudden inrush of blood occurs, the needle should be withdrawn and inserted into another location. After penetrating a centimeter or so into the expected depth of the tumor, the needle should be turned and while releasing suction it should be slowly withdrawn.—*A. A. de Lorimier.*

COCCHI, UMBERTO. Kurzer Beitrag zur Frage der Leukoplakie, Syphilis und malignem Tumor. (Short contribution to the question of leukoplakia, syphilis and malignant tumor.) *Strahlentherapie*, 1940, *68*, 522–529.

It was formerly thought that leukoplakia was pathognomonic of syphilis, but now this is not generally accepted. The author reports examinations of the mouth in 1,988 patients and gives a table showing the details in regard to the finding of leukoplakia, syphilis and malignant tumor. It was impossible to decide definitely for or against a relationship between leukoplakia and syphilis. The majority of the patients with leukoplakia had not had syphilis. No statistical relationship between syphilis and malignant tumor could be demonstrated. The coexistence of syphilis and malignant tumor is accidental. This is true of malignant tumors of the mouth as well as of tumors in other locations.

No definite relationship between malignant tumor and leukoplakia can be demonstrated statistically. Leukoplakia is not a necessary preliminary condition to malignant tumor nor are they necessarily associated.

But it cannot be denied that leukoplakia does occasionally undergo malignant degeneration and to this extent may be considered precancerous. It is not known how frequent this

malignant degeneration is or whether it is of any statistical importance. But leukoplakia is to be considered a serious condition on account of the fact that it does undergo malignant degeneration, even though only rarely, and patients with leukoplakia should be given periodical examinations in order that malignant degeneration may be detected early if it occurs.—*Audrey G. Morgan.*

Kolbow, Heinrich. Dosisersparnis durch Anwendung härterer Strahlung in der Röntgendiagnostik als Ergebnis intravaginaler Dosismessungen. (Decreasing the dose by the use of harder rays in roentgen diagnosis as shown by intravaginal measurements of dosage.) *Strahlentherapie*, 1940, *68*, 620–644.

The author discusses the disputed question of whether the growing embryo can be injured by irradiation of the mother's body during pregnancy. He agrees with the conclusions of Timoféeff-Ressovsky that the fetus cannot be directly injured but concedes that it may be possible to injure the germ plasm and cause injury in later generations by the application of too large doses of radiation to the ovaries.

Such an injury of the germ plasm depends on the size of the dose applied to the ovaries. The necessary condition for the avoidance of injury is to use a technique that will apply as small a dose as possible. The best way to reduce the dosage is to use harder rays, which can be done without any essential injury to the quality of the roentgenogram. The usual dosage used heretofore in taking roentgenograms of the pelvis has been 0.1 to 0.3 r for roentgenograms and about 0.5 r/min. for roentgenoscopy. By increasing the tension heretofore used by 10 kv. and using an additional filter of 2 mm. aluminum the intravaginal dose can be reduced to one-half or even one-third and that for roentgenoscopy by about one-third. A wealth of detail is given in regard to the technique of intravaginal measurement of the dosage and tables showing the author's results and those of other investigators.

The question still remains whether the very small doses now in use can injure the germ plasm. Theoretically any amount of radiation can cause some degree of biological injury but it is probable that the small doses now in use do not do any injury that is of any practical importance. The limit at which practical injury begins has not yet been worked out definitely, but it is probably not reached even with repeated exposures with the dosages that can now be used.

In the anxiety to avoid injury it is not necessary to avoid taking the number of roentgenograms required for accurate diagnosis nor to avoid methods of examination that are valuable clinically such as salpingography and roentgenograms during pregnancy. Instead of avoiding necessary examinations effort should be directed toward using a technique that is adapted to the examinations required. One roentgenogram with wrong technique may do more harm than a series with the best available technique.—*Audrey G. Morgan.*

Grynkraut, B. De la dose thérapeutique dans le traitement des tumeurs malignes. (The therapeutic dose in the treatment of malignant tumors.) *J. de radiol. et d'électrol.*, May, 1939, *23*, 203–206.

The premise is made that the therapeutic dose consists of the following two parts: (1) the direct or sterilizing (method of Chaoul)—small surface, feeble penetration and fractionation for superficial tumors; (2) the indirect or sensitizing or method of Mallet—large surface, strong penetration, feeble dose and slow r per minute.

The direct dose is said to stop cellular growth. Numerous experiments by various investigators using tissue cultures showed that the sterilizing dose equals from 25,000 to 30,000 r given at one time no matter what the wave length or type of tissue (normal, benign or malignant) may be. The important point is that living cells are necessary. A cell only becomes radiosensitive within the organism. This radiosensitivity is not permanent. It may disappear under the influence of repeated irradiation (secondary radioresistance) or as a radioresistant metastatic ganglion.

A theory is postulated concerning the existence of sensitizing.

The following conclusions are drawn from the various experiments:

(1) A radioresistant tumor may be cured by applying a sterilizing dose (direct) employing small fields, provided that the tumor is at or near the surface.

(2) Large surface irradiation sensitizes because of the indirect dose. Therefore it is advisable to use a grid with the resultant division into numerous small fields.

(3) The therapeutic dose consists of both a direct, sterilizing dose and an indirect, sensitizing dose. The latter decreases and the former increases as the portal is made larger.

(4) The time factor is also important as shown by transplantation experiments in which the tumors that remained longest in the irradiated field grew poorly after transplantation. This contrasted with the tumors that were removed early.

(5) It is plausible that certain growth substances exist as simple pericellular debris which at times possess the power of fluorescence. Tumors developing during this fluorescent stage would be radiosensitive. In the non-fluorescent stage the tumor would be radioresistant as is every cell outside of the organism.—*M. L. Sussman.*

NØRGAARD, FLEMMING. The development of fibrosarcoma as a result of the intra-articular injection of radium chloride for therapeutic purposes; a new form of radium poisoning in human beings. *Am. J. Cancer*, Nov., 1939, *37*, 329–342.

The benefits obtainable with the proper usage of radium are well known; likewise the malresults: local burns, changes in the hemopoietic system, sterility and fibrosis in parenchymatous organs. Blum, Hoffman, Martland, and others, have reported osteitic changes and bone necroses as well as sarcomatous changes because of the intake of radium salts either by occupational activities or as a result of imbibing radioactive waters for medicinal purposes.

The author is reporting one case of such unfortunate consequences. The patient was a female, aged fifty-six, who was admitted because of a tumor in her right knee. She had had arthritic symptoms since the age of eleven. In 1928 she received treatment at the radium springs at St. Joachimstal, Bohemia, with spectacular improvement. These treatments were therefore repeated in 1929, 1931, 1934 and 1937. In September, 1937, intense pain developed in the right knee. Roentgenography, accomplished a year later, revealed almost total destruction of the upper end of the tibia with some irregular new bone formation and with flattening of the head and a compression fracture. There was marked swelling of the soft tissues. Various manifestations of arthritis were visualized in other joints. Biopsies failed to reveal neoplastic cells but showed necrotic bone cells. It was learned that in 1928 a radium injection was given into the right shoulder joint, while in 1929 two more were given into the right knee. Geiger counter tests revealed radioactivity in the right shoulder and in the right knee. An arthrotomy was performed and histological studies revealed a spindle cell sarcoma and fibrosarcoma. The radium content of the ash was found to be equivalent to 3×10^{-4} micrograms of radium. By correspondence, it was learned that approximately 3.64 micrograms of radium had been injected into the knee and that a total of 10 micrograms had been injected in or about the joints.

Various observations have indicated that following an intake of radium a large percentage of it is immediately excreted but that the rest of it becomes firmly fixed to tissue, particularly to bone and that thereafter the rate of excretion is negligible even throughout a lifetime.

The dangers of all internal radium administrations are therefore emphasized. Agreement is expressed to the expression of Fleming and Chase in discouraging the use of thorium dioxide for patients who are expected to live as long as two years. Explanation of the damage is believed to be attributable to the effects of the alpha particles—accounting for 90 per cent of the radiation emitted (Martland).—*A. A. de Lorimier.*

LABORDE, S. Les dangers des substances radioactives introduites dans l'organisme. (The dangers of radioactive substances introduced into the body.) *Presse méd.*, March 15, 1939, *47*, 393–394.

The author considers particularly the skin injuries resulting from this procedure and excludes from consideration the affinity of the substances for the osseous system and more particularly for the reticulo-endothelial system. These injuries are not rare; they probably occur more often than might be judged from the literature. Most cases result from the injection of salts of mesothorium and are attributed to local retention. It is thought ordinarily that these salts are dangerous because mesothorium has a half life of twenty years. The dangers of thorium X are minimized because its half life is about three and a half days. This is a mistake because severe biologic effects may result from the rapid reduction of considerable energy. The question arises as to why injections of comparable doses result in differing manifestations.

An explanation might be afforded by a case in which a series of intermuscular injections of thorium X were given corresponding to a total dose of 1 mg. of actual substance. This is a fairly large dose but is not considered excessive. Ten years later a deep induration could be palpated which had persisted since the end of the treatment. The area was reddened and spontaneously a whitish material was extruded from a sinus tract. Cicatrization occurred progressively until finally a small fistula remained. The area was painful and roentgen examination revealed opaque material. The patient was pale and complained of marked fatigue. A mild anemia was found with a marked leukopenia. Mononucleosis was present but not more than is often found in the presence of anemia. It appears that the tissues were subjected to an intense bombardment with alpha and beta rays for several months. It seems probable that radioactive substances of long life were mixed with a solution of thorium X in the injected material. The area of radiodermatitis and the adjacent opaque substance was excised. The surgeon found in the skin and a large part of the adipose tissue an encrusted hard, white material appearing calcific corresponding to the area localized by the roentgen examination. Chemical examination revealed calcium phosphate and traces of carbonates. There was 29 per cent calcium. Spectrographic examination showed no thorium but demonstrated the presence of calcium and magnesium. Histologically a typical atrophic radiodermatitis was found. The stratum granulosum had disappeared along with the presence of hyperkeratosis. The epithelium was atrophied and irregular; in some few areas there was hyperplasia. The subepithelial layers were dense and sclerotic with small lymphoid islands. In addition, in the adipose tissue there were pseudocystic areas of irregular contour. They appeared necrotic with some evidence of lipophagocytosis. In some areas there were rounded vacuoles which were more or less filled with a brown amorphous substance which was negative on examination with polarized light. Peripherally there was a fine calcific capsule surrounded by an area of fibrosis. An analysis of the radioactivity led to the conclusion that these salts could result in effects a long time afterwards because all that was not eliminated was insoluble and acted, therefore, like a soluble salt remaining for a long time at the point of origin. The general conclusions reached, therefore, were that although soluble radioactive salts are chosen because of their rapid elimination a certain quantity of active material persists and is sufficient to cause local tissue changes. Furthermore, it appeared that the product injected was not thorium X exclusively but also contained mesothorium and radium.—*M. L. Sussman.*

Wolf, Karl. Über die vakuolige Degeneration der röntgenbestrahlten Karzinomzellen. (Vacuolar degeneration of carcinoma cells irradiated with roentgen rays.) *Strahlentherapie*, 1940, *68*, 688–693.

The author describes the histological findings in a case of carcinoma of the skin. The patient was a woman of sixty-seven who had had a small tumor of the cheek for five years. It was excised in 1936 and recurred in the scar in 1938. Histological examination of the excised tumor had shown pavement cell carcinoma. The recurrence was given fractional irradiation of 800 to 850 r from four directions, amounting to a focal dose of 325 per cent skin erythema dose. Three months later the tumor had decreased to the size of a cherry and a dosage of 320 per cent skin erythema dose was given. Eight months after the beginning of the first irradiation and five months after the second the tumor had broken down in the middle and the opening reached to the mucosa of the mouth. Pieces were excised, sectioned and examined.

In the cell nuclei there were small vesicles containing fluid which became confluent and formed larger ones. The walls of the nuclei burst and the fluid flowed into the cytoplasm. The degeneration with large vesicles which is always seen in cells severely injured by irradiation had affected the cell nuclei also. After evacuation of the vacuoles the nuclei became pyknotic. In cells that are injured by irradiation the injury of the nucleus is the most striking phenomenon; the other changes in the cell body are probably only effects of this.—*Audrey G. Morgan.*

Kasabach, Haig H., and Merritt, Katharine K. Capillary hemangioma with extensive purpura. *Am. J. Dis. Child.*, May, 1940, *59*, 1063–1070.

Kasabach and Merritt report a case of extensive hemangioma of the skin associated with diffuse purpuric manifestations. At the age of two and three-quarter months, the hemangioma involved the left leg, the scrotum and the abdomen. From April 21 to July 1, 1937, the pa-

tient received seventeen roentgen treatments. In view of the low platelet count and because of the extensive nature of the hemangioma, small doses were administered and the affected region was divided into six small fields varying from 6 by 8 to 10 by 10 cm. At the beginning of the course only one area was treated at daily intervals. From June 1 on, the treatments were separated by intervals of three or four days. Only on three occasions a field of 10 by 15 cm. was used on ulcerated areas over the posterior medial aspect of the left thigh. The technical factors were: 130 kv., 4 ma., 27 cm. distance and a filter of 3 mm. of aluminum. The quantity varied from 75 to 100 roentgens (measured in air) per sitting per field. This plan was continued over a period of nine weeks until each of the six fields had received approximately 300 roentgens, measured in air. The lower part of the abdomen and the genitalia were not included in the fields of irradiation.

On July 8, 1937, seven 4.4 cm. and six 3.2 cm. radium needles were inserted in and around the ulcerated hemangiomatous lesion on the posteromedial aspect of the thigh so as to produce uniform irradiation. The dose was estimated to be about 6 milligram-hours per square centimeter. The total dose of interstitial irradiation over an area of 7.7 by 17.8 cm. was 878.84 mg-hr.

Though the lesion was seemingly malignant, the results of biopsy did not substantiate this clinical impression, nor has the patient's course. The authors feel fairly certain, therefore, that the lesion was benign, although it is impossible to say whether the combined roentgen and radium treatment was the deciding factor in combating a lesion which was or might have become malignant. The treatment count was continued even though the platelet count was low.

On June 2, 1939, roentgenograms of the pelvis and extremities were made which showed no disproportion in the width and length of the bones on the two sides. The ossification centers were symmetric. No evidence of retardation of growth was demonstrated.

At two and one-half years of age the patient was in good health. The discoloration and swelling had greatly decreased. The scar in the left upper medial thigh was firm, inelastic, adherent and interfered slightly with the action and elasticity of adduction and with the function of the medial ham string muscles. The gait was normal.

To the authors it seems reasonable to state that the judicial application of roentgen and radium therapy in small doses to a hemangioma with purpura has no deleterious effect on the low platelet count. The great importance of a biopsy of a lesion as extensive as the one reported is strongly emphasized.—*R. S. Bromer.*

SCHAEFER, FELIX. Röntgennahbestrahlung bei Blutgefässgeschwülsten (Hämangiomen). (Close roentgen irradiation in blood vessel tumors—hemangiomas.) *Strahlentherapie*, 1940, *68*, 518–521.

War conditions have necessitated the use of many materials, including radium, for war purposes. Therefore the use of the close method of roentgen irradiation has been substituted for radium treatment of hemangiomas. In some respects it has proved equal to and in some even superior to the use of radium needles.

The author reports the treatment of 52 cases since June, 1939. Of course the time has been too short for the reporting of final results. The apparatus used was a small one that can be attached to any light outlet. It is thrown over the shoulder and held with one hand while the other holds the tube. The focus of the tube can be brought to within 2 cm. of the surface of the skin. At this distance and with 50 kv. the tube yields 8,136 r per minute. The quality of the rays can be changed by increasing the distance or using a filter of 1 to 2 mm. aluminum. The round outlet for the rays has a diameter of 0.5 to 2.5 cm. If the tumor is larger than that it can be divided into several fields.

This method has the advantage over radium treatment that it is much simpler. No anesthesia is necessary and the treatment can be given in the office. It lasts only a few seconds, which is a great advantage in the treatment of restless young children.

Among these 52 hemangiomas 16 have been cured, 22 improved, that is the tumor became flatter and paler, and 14 have showed only slight improvement. The reason for the small number of cures is that in most of the cases the treatment has not yet been completed. The irradiation has to be repeated three or four times.

At first doses of 1,100 r were given, 50 kv., 2 cm. distance and no filter. This was found to produce quite a severe inflammation at first, so the dose was reduced to 550 r. With this dose the tumor recedes gradually and without any violent reaction. The method does not seem to

be particularly well adapted for very large tumors.—*Audrey G. Morgan.*

Heeren, J. G. Röntgenbestrahlung in Kombination mit Ultrakurzwellen und Insulininjektion. (Roentgen irradiation combined with ultrashort wave irradiation and insulin treatment.) *Strahlentherapie*, 1940, *68*, 444–459.

The greater curability of carcinomata of the uterus is probably due largely to their better blood supply. Tumors of the esophagus and stomach are particularly unfavorable in this respect. The association of short wave treatment with roentgen irradiation helps to improve the blood supply. Insulin injections seem to increase the permeability of the tumor cells and therefore increase the effectiveness of irradiation.

The author reports 27 cases in which he has used this combined treatment since 1936; there were 7 carcinomata of the esophagus, 15 of the stomach, 1 mediastinal tumor, 3 carcinomata of the lungs and 1 of the rectum. The patients were given short wave treatments for ten to fifteen minutes before and after roentgen irradiation. They were also given 10 to 15 units insulin generally immediately before or after the roentgen treatment. The roentgen treatment was given by Holfelder's method, with 60 per cent of a skin erythema dose per field daily with the cross-fire technique; 180 kv., 4 ma., distance 40 cm., skin erythema dose 550 r, measured in air.

All of these patients were in practically a hopeless condition before treatment; treatment was given only to control pain and for psychic reasons. Nevertheless the condition of most of them was greatly improved. Not only was there subjective improvement but in many cases a marked gain in weight. That this was not due merely to water retention from the insulin treatment was shown by the fact that there was an increase of hemoglobin. The improvement was greater in the cases in which short wave treatment and insulin both were given than in the ones where the only supplementary treatment was short wave irradiation. This was particularly true in carcinoma of the stomach. One case of inoperable carcinoma of the rectum has been kept stationary for a year and a half. The tumor has also decreased in size and the general condition has been satisfactory. The size of the tumors was decreased in a number of the cases. The treatment did not have any unfavorable effects in any case.—*Audrey G. Morgan.*

Ash, J. E. Epithelial tumors of the bladder. *J. Urol.*, Aug., 1940, *44*, 135–145.

There are now over 3,200 cases in the Bladder Tumor Registry of the American Urological Association. Males are afflicted 3 times as commonly as females. Over 80 per cent of the tumors have occurred past the age of fifty. Hematuria has been the primary symptom in 75 per cent of cases. Over two-thirds of the tumors are located in the posterior wall, including the trigone and neck. Bladder tumors are comparatively benign but lead to serious complications. Only 12 per cent of the group have shown metastasis. Most cases die of infection. There are two morphological groups, the sessile infiltrating, and the papillary. The latter are by far the most common, probably 80–90 per cent. The author grades them according to Broders' classification. In Grade 1 the transitional cell is present, mitoses are infrequent and there is no evidence of invasion. Some call these simple papilloma. In Grade 2 there is no uniformity of cell type or arrangement, mitoses are frequent and invasion may or may not occur. Grades 3 and 4 show greater anaplasia, metaplasia and frank invasion. While admitting that benign papillomas occur, the author does not feel that he can make the diagnosis with certainty. Benign papillomas are also prone to recur and may cause as serious complications as the more malignant types.

When metastasis does occur it is to the regional lymph nodes and bones, especially the pelvic girdle and vertebrae.

In regard to treatment, the author has noted in going over the registered cases the severity of secondary reactions following deep roentgen therapy. In comparing irradiated and non-irradiated cases any difference in outcome was in favor of the non-irradiated cases. He advises against routine irradiation in view of the radioresistance of most bladder tumors and the possibility of serious post-irradiation damage. He advises surgery, including fulguration, as the ideal treatment.—*R. M. Harvey.*

Colby, F. H. Supervoltage radiation in the treatment of bladder tumors. *J. Urol.*, Aug., 1940, *44*, 216–222.

The author presents a case of a man, aged fifty-eight, with hematuria and lower abdomi-

nal pain. Cystoscopic examination showed an extensive infiltrating bladder growth at the base. The cystogram was normal. Biopsy showed an undifferentiated epidermoid carcinoma, Grade 3. From November 25 to December 17 he received 2,400 r of supervoltage radiation to each of three pelvic portals, 12 × 12 cm., anterior, and posterior right and left oblique, in daily doses of 400 r, and 600 r to each of two lateral ports. This made a total of 8,400 r to the skin. After 7,200 r he had considerable frequency and passed purulent sloughing material in the urine. Forty days later he had no frequency or hematuria and cystoscopic examination showed no tumor. No slough could be seen and the mucous membrane appeared intact. He received an additional 1,200 r to the three pelvic portals and 600 r to the two lateral portals five weeks after completion of the original series. Six weeks later he had only moderate bladder irritability and a biopsy showed no tumor tissue.

The results of treating 24 bladder tumors, unsuited to surgery, with million volt therapy is discussed. Fifty per cent of the cases were papillary carcinoma Grade 2 and 33.3 per cent infiltrating carcinoma Grade 3. Total skin dosage varied from 4,200 to 22,800 r. Twelve patients received over 8,000 r. The average course was as outlined in the case presented above. The filtration was 5 mm. of lead; half-value layer 11 mm. of copper; focal skin distance 70 cm. Definite regression occurred in 75 per cent of the Grade 3 undifferentiated carcinomas and in 16 per cent of the papillary tumors. In 7 patients tumor could be seen with the cystoscope after treatment. Only one of these had had any previous treatment. The tumor recurred in 4 and 2 of these died of cancer. Metastasis was found in the fifth at autopsy and one of the remaining 2 is evidently dying of cancer. Only one of the 7 cases in whom no tumor could be identified by cystoscope remains well without evidence of tumor, although it has only been two months since his last series was completed. A majority of the patients received marked symptomatic relief.

In conclusion, it seems evident that supervoltage roentgen therapy offers little in the way of cure of malignant bladder tumors. The method is recent, however, and the dosage not yet fixed. Disappearance of the tumor has occurred grossly more frequently with this method than with other methods of external irradiation, although viable cancer cells seem to persist in the bladder wall. The author advises the treatment only in advanced tumors or where surgery is contraindicated, feeling that surgery is still the method of choice.—*R. M. Harvey.*